Subs., anhydrous, 0.1132: 11.4 cc. N (20.0°, 758 mm.). Subs., 0.2586: $Mg_2As_2O_7$, 0.1123.

Calc. for $C_{10}H_{13}O_5N_3AsNa$: N, 11.90; As, 21.22. Found: 11.71; As, 20.96.

N-**(3-Methylphenyl-4-arsonic acid)glycine-methylureide.**—After one hour 23 g. of 3-methyl-4-aminophenyl arsonic acid as the sodium salt and 15 g. of α-chloroacetyl-β-methyl-urea yielded a solution which set to a thick, crystalline mass on cooling. This was diluted with water and treated with 40 cc. of 10% hydrochloric acid. Reprecipitated from hot dil. ammoniacal solution with acetic acid, the yield was 12 g. The substance is sparingly soluble in hot water but dissolves in boiling 50% alcohol. It separates from the former as hair-like needles and from the latter as radiating masses of minute needles. When rapidly heated it decomposes at 218–9°.

Subs., 0.1326: 14.0 cc. N (24.5°, 756 mm.). Subs., 0.3418: $Mg_2As_2O_7$, 0.1523.

Calc. for $C_{11}H_{16}O_5N_3As$: N, 12.17; As, 21.72. Found: N, 12.07; As, 21.52.

N-**(2-Hydroxyphenyl-5-arsonic acid)glycine-ureide.**—On boiling a solution of 3.8 g. of 3-amino-4-hydroxyphenyl arsonic acid[1] in 16.5 cc. of *N* sodium hydroxide solution with 4.4 g. of chloroacetyl-urea it suddenly set to a solid, crystalline cake. After another hour on the water bath water was added and the crystalline mass disintegrated and filtered. Reprecipitated from solution in hot, dil. ammonia with acetic acid, the substance separated as flat, minute, almost colorless, glistening needles which contained between 1 and 1.5 molecules of water of crystallization. The yield was 3.3 g. When anhydrous it decomposes at 203–5°.

Subs., air-dry, 0.4214: loss, 0.0257 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_9H_{12}O_6N_3As.H_2O$: H_2O, 5.13. Found: 6.10.

Subs., anhydrous, 0.2946: (Kjeldahl) 26.65 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1380.

Calc. for $C_9H_{12}O_6N_3As$: N, 12.62; As, 22.50. Found: N, 12.68; As, 22.61.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

AROMATIC ARSENIC COMPOUNDS. IV.

AROMATIC AMIDES OF *N*-ARYLGLYCINE ARSONIC ACIDS.

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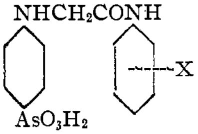
In continuation of the studies described in the preceding papers of this series,[2] we have prepared the arylamides and substituted arylamides of the arylglycine arsonic acids possessing the following general formula:



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[1] THIS JOURNAL, 40, 1590 (1918).

[2] *Ibid.*, 41, 1581, 1587, 1600 (1919).

a series of compounds with such extensive synthetic possibilities as to afford a very fertile ground for chemotherapeutic researches.[1]

Like the alkylamides and ureides these substances were readily obtained by the interaction of the sodium salt of the aminoaryl arsonic acid with the aromatic chloroacetylamino compound, according to the reaction $NaHO_3AsC_6H_4NH_2 + ClCH_2CONHAr \longrightarrow H_2O_3AsC_6H_4NHCH_2CONHAr + NaCl$. In the case of the chloroacetyl derivatives of the simpler amines or of their halogen, nitro, acylamino, carboxamide, carboxureide, or sulfonamide derivatives, the reaction was best accomplished in 50% alcoholic solution in the presence of sodium iodide, the latter causing the intermediate formation of the more reactive iodoacetyl compounds. However, where chloroacetylamino acids or the simpler chloroacetyl-aminophenols were employed the condensation could be carried out rapidly in aqueous solution without the use of sodium iodide. In such cases, one-half to one hour's boiling usually sufficed for complete reaction owing to the great lability of the chlorine in these compounds, whereas the chlorine in the first mentioned substances is far more stable. On boiling the chloroacetylamino acids or phenols with aqueous alkali or salts of weak acids a copious liberation of chlorine ion may quickly be obtained, whereas such a result can be obtained with the chloroacetyl compounds of other aromatic amines only through much more vigorous treatment.

In some instances the great reactivity of these chloroacetyl compounds produced complications, since the sodium arsanilate functioned rather as a salt of a weak acid and removed the chlorine before much opportunity for condensation with the amino group was afforded. This difficulty was overcome in the case of chloroacetyl-anthranilic acid by the use of its ethyl ester and subsequent saponification of the resulting ester arsonic acid. It was also found necessary to adopt a similar procedure in the case of chloroacetyl-methylanthranilic acid. A similar difficulty was encountered in using *o*-chloroacetylamino-phenol for the preparation of the *o*-hydroxyanilides, on account of the readiness with which it undergoes *ortho* condensation in the presence of salts of weak acids to form the anhydride of *o*-amino-phenoxyacetic acid. This reaction preponderated particularly with *o*- and *p*-arsanilic acids and only poor yields of the desired glycine compounds were obtained. The yields were greatly improved, however, by employing two molecules of arsanilic acid itself instead of the sodium salt, the formation of *o*-amino-phenoxyacetic anhydride being almost completely suppressed.

The reaction with *o*-chloroacetylamino-phenol also afforded an interesting opportunity to note the differences in reactivity between *m*-arsanilic

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[1] Cf. footnote, THIS JOURNAL, 41, 1588–9 (1919).

acid on the one hand and the *o*- and *p*-acids on the other. It has been our experience that amines with negative substituents such as *m*-nitraniline react more readily with halogen-acetyl compounds than do the *o*- and *p*-isomers. In the reaction between sodium *m*-arsanilate and *o*-chloroacetylamino-phenol the tendency toward glycine formation was such as to proceed at a more rapid rate than the formation of *o*-amino-phenoxyacetic anhydride, so that the yield of the *o*-hydroxyanilide was much greater and that of the by-product much smaller than in the case of the isomeric arsanilic acids. It is probable that a comparative study of the reactivity of the aminophenyl arsonic acids with other halogen-acetyl compounds would yield a similar result. Such experiments involving velocity measurements were, however, beyond the scope of the present studies.

Special attention has been given in the present work to a study of the hydroxyanilides of the arylglycine arsonic acids, since reduction converts them into a group of arseno compounds which yield water-soluble alkali phenolates. These trivalent arsenicals have been the subject of interesting biological investigations and since both the chemical and biological studies with such compounds are still in progress, their description will be left to later communications.

As derivatives of the phenylglycine arsonic acids, the substances herein described function both as acids and bases. As acids they are easily displaced from their salts by acetic acid, except in those cases in which the arylamide nucleus is substituted by other acid groups, in which case either a mineral acid or a large excess of acetic acid is required. The feeble basic properties due to the imino group are typified by the formation of hydrochlorides only in the presence of relatively strong hydrochloric acid. As secondary amines they also yield nitroso derivatives. The amide linkage renders the glycineanilides susceptible to hydrolysis on boiling with mineral acids or alkalies, but they seem somewhat more stable toward the action of alkali than the corresponding aliphatic amides.

As a rule the free arsonic acids do not possess sharp melting or decomposition points, the values obtained depending greatly upon the rate of heating. They are on the whole but sparingly soluble in the usual solvents. The sodium salts, on the other hand, dissolve more or less readily in water depending upon the nature and position of the substituting groups and are often salted out by sodium chloride or acetate. For the convenience of biological testing the sodium salts were prepared in many cases, although this was also found a convenient means for the purification of individual compounds.

EXPERIMENTAL.

(A) Derivatives of *p*-Arsanilic Acid.

***N*-(Phenyl-4-arsonic Acid)glycineanilide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_5$.—This substance can be prepared by the two methods already described in the preparation of the amide of phenylglycine-*p*-arsonic acid;[1] *viz.*, by the reaction of sodium arsanilate with chloroacetanilide or by that of phenyl-(4-arsonic acid)-glycine methyl ester with aniline itself. Both the speed and yield of the first reaction are much improved either by replacing the chloro compound by the iodoacetyl derivative or by adding sodium iodide to the reaction mixture.

22 g. of arsanilic acid were dissolved in 100 cc. of *N* sodium hydroxide solution. To this were added 17 g. of chloroacetanilide,[2] 20 g. of sodium iodide, and 100 cc. of alcohol and the mixture was boiled for two hours. During the heating the reaction product suddenly separated. After cooling the substance was filtered off, washed with 50% alcohol and redissolved in dil. ammonia. On reprecipitating the hot solution with an excess of acetic acid, the arsonic acid separated in easily filterable form in a yield of 25 g. Recrystallized from 50% alcohol it separates as minute, delicate needles which do not melt below 285° when rapidly heated. As a secondary amine it reacts with nitrous acid, giving the nitroso derivative described below. The substance is practically insoluble in the cold in the usual organic solvents, but is appreciably dissolved by a large volume of hot methyl or ethyl alcohol or glacial acetic acid. It is insoluble in cold dil. hydrochloric acid, but on warming it dissolves, forming the hydrochloride, which separates on cooling.

Subs., 0.1308: 9.05 cc. N (22.0°, 763 mm.). Subs., 0.4164: $Mg_2As_2O_7$, 0.1828.
Calc. for $C_{14}H_{15}O_4N_2As$: N, 8.00; As, 21.39. Found: N, 8.04; As, 21.18.

The substance was also prepared as follows: 6 g. of (phenyl-4-arsonic acid)-glycine methyl ester[3] and 12 g. of aniline were treated with 20 cc. of methyl alcohol and heated on the water bath until solution was complete. The alcohol was then allowed to boil off and after several hours' heating the melt began to crystallize. The residue was finally taken up in dil. sodium hydroxide solution, and made definitely alkaline to phenolphthalein to saponify any unchanged ester. The filtered solution was then acidified with acetic acid and on scratching the arsonic acid separated and was purified as above described. The substance so obtained agreed in all of its properties with that obtained by the alternative method.

Subs., 0.1549: 10.6 cc. N (24.5°, 754 mm.).
Calc. for $C_{14}H_{15}O_4N_2As$: N, 8.00. Found: 7.79.

Sodium Salt.—On dissolving the arsonic acid in dil. sodium hydroxide

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[1] THIS JOURNAL, 41, 1589 (1919).

[2] *Ibid.*, 39, 1441 (1917).

[3] *Ibid.*, 41, 1590 (1919).

solution until faintly alkaline to litmus and adding an equal volume of saturated sodium acetate solution, the sodium salt separated as glistening scales. After filtering and washing with 20% sodium acetate solution, and then with 85% alcohol, it was air-dried. The salt contained 4 molecules of water of crystallization. It is freely soluble in water and its dilute solutions do not give immediate precipitates with calcium or barium salts. With magnesia mixture a precipitate is formed only on heating, while heavy metal salts give insoluble precipitates at once.

Subs., air-dry, 0.9416: Loss, 0.1553 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{14}O_4N_2AsNa.4H_2O$: H_2O, 16.22. Found: 16.49.
Subs., anhydrous, 0.1709: 11.4 cc. N (21.0°, 754 mm.).
Calc. for $C_{14}H_{14}O_4N_2AsNa$: N, 7.53. Found: 7.69.

Nitroso Compound, *p*-$H_2O_3AsC_6H_4N(NO)CH_2CONHC_6H_5$.—3 g. of the arsonic acid were suspended in 35 cc. of glacial acetic acid and treated slowly, with constant agitation, with 6 cc. of a 10% sodium nitrite solution. Only a portion of the substance dissolved and the mixture was heated to boiling, forming a clear, yellow solution. To complete the reaction 0.5 cc. of sodium nitrite solution was added and the mixture cooled, rosets of flat needles forming on scratching. After dilution with water to complete the separation the nitroso compound was filtered off and recrystallized from 50% alcohol. It separated as sheaves of long, flat, colorless needles containing one molecule of water of crystallization. The yield was 2.3 g. When rapidly heated to 185°, then slowly, it effervesces at 190–2°. It is very sparingly soluble in boiling water, readily in boiling 50% alcohol, quite easily in the cold in acetic acid, and somewhat sparingly so in cold 95% alcohol. The nitroso compound is turned brown by sulfuric acid but dissolves to a colorless solution; in the presence of phenol, however, a brown solution is obtained, changing rapidly to deep green.

Subs., air-dry, 0.4429: Loss, 0.0218 *in vacuo* at 80° over H_2SO_4.
Subs., 0.1023: 9.5 cc. N (24.0°, 761 mm.). Subs., 0.2979: $Mg_2As_2O_7$, 0.1154.
Calc. for $C_{14}H_{14}O_5N_3As.H_2O$: H_2O, 4.54; N, 10.58; As, 18.87. Found: H_2O, 4.92; N, 10.69; As, 18.70.

***N*-(Phenyl-4-arsonic Acid)-glycine-2′-toluidide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_3$(*o*-).—This substance was prepared as usual from chloroacetyl-*o*-toluidine, aided by the addition of sodium iodide. Purified by redissolving in a slight excess of dil. sodium hydroxide solution, warming, and reprecipitating with acetic acid the acid separated slowly as aggregates of flat, microscopic needles. Recrystallized from 50% alcohol it forms woolly masses of delicate needles which do not melt below 275° and are sparingly soluble in hot water and acetone. It is insoluble in the cold in 50 or 95% alcohol but appreciably so on boiling and readily so in hot acetic acid. It dissolves appreciably in cold methyl alcohol.

Subs., 0.2944: 9.9 cc. N (24.5°, 758 mm.).
Calc. for $C_{15}H_{17}O_4N_2As$: N, 7.69. Found: N, 7.69.

Sodium Salt.—On adding several volumes of alcohol to the neutral solution of the acid in dil. sodium hydroxide the sodium salt separates slowly as aggregates of long, narrow platelets which contain 2.5 molecules of water of crystallization.

Subs., air-dry, 0.5627. Loss, 0.0580 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{16}O_4N_2AsNa.2.5H_2O$: H_2O, 10.44. Found: 10.31.
Subs., anhydrous, 0.2944: (Kjeldahl), 15.0 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1175.
Calc. for $C_{15}H_{16}O_4N_2AsNa$: N, 7.26; As, 19.41. Found: N, 7.14; As, 19.27.

***N*-(Phenyl-4-arsonic Acid)-glycine-3′-toluidide.**—The yield from 3.7 g. of chloroacetyl-*m*-toluidine[1] was 4 g. The crude product was recrystallized from 85% alcohol, separating as aggregates of long, thin plates. When rapidly heated it decomposes at about 285°, with preliminary darkening and softening. It is insoluble in boiling water or acetone, but is appreciably soluble in boiling methyl and ethyl alcohols and readily so in boiling acetic acid.

Subs., 0.1929: 13.3 cc. N (22.5°, 764 mm.). Subs., 0.3012: $Mg_2As_2O_7$, 0.1257.
Calc. for $C_{15}H_{17}O_4N_2As$: N, 7.70; As, 20.58. Found: N, 8.01; As, 20.16.

***N*-(Phenyl-4-arsonic Acid)-glycine-4′-toluidide.**—This substance, obtained from chloroacetyl-*p*-toluidine, separates from the reaction mixture during the heating. Reprecipitated with acetic acid from its solution in sufficient hot, dil. sodium hydroxide it separated as minute aggregates of short, flat, microscopic needles. It crystallizes from hot 50% alcohol, in which it is but sparingly soluble, as woolly masses of minute needles which do not decompose when heated up to 280°. It is practically insoluble in boiling water, and but sparingly so in boiling methyl or ethyl alcohol but is readily soluble in boiling acetic acid.

Subs., 0.1496: 9.8 cc. N (25.0°, 762 mm.).
Calc. for $C_{15}H_{17}O_4N_2As$: N, 7.69. Found: 7.53.

Sodium Salt.—When the acid is dissolved in hot, dil. sodium hydroxide solution and carefully neutralized with acetic acid the sodium salt separates on cooling as long, thin, curved, glistening needles, containing three molecules of water of crystallization. This salt is sparingly soluble in cold water and even less so in the presence of other sodium salts.

Subs., air-dry, 0.6936: Loss, 0.0856 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{16}O_4N_2AsNa.3H_2O$: H_2O, 12.28. Found: 12.34.
Subs., anhydrous, 0.2989: (Kjeldahl), 15.3 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1213.
Calc. for $C_{15}H_{16}O_4N_2AsNa$: N, 7.26; As, 19.41. Found: N, 7.17; As, 19.59.

***N*-(Phenyl-4-arsonic Acid)-glycine-α-naphthylamide,** p-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_{10}H_7(\alpha$-$)$. — Chloroacetyl-$\alpha$-naphthylamine reacted smoothly, the product separating from the clear solution on scratching. It was best purified by precipitating a hot, dil. ammoniacal

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[1] *J. Biol. Chem.*, **21**, 108 (1915).

solution with acetic acid, forming aggregates of microscopic needles. It is practically insoluble in boiling water or 50% alcohol. When rapidly heated it darkens slightly, but does not melt up to 280°. On heating its solution in dil. sodium hydroxide the odor of α-naphthylamine is quickly noticeable owing to slight cleavage of the amide linking.

Subs., 0.1466: 9.0 cc. *N* (22.0°, 758 mm.). Subs., 0.3799: $Mg_2As_2O_7$, 0.1457.
Calc. for $C_{18}H_{17}O_4N_2As$: N, 7.00; As, 18.73. Found: N, 7.09; As, 18.51.

N-**(Phenyl-4-arsonic Acid)-glycine-β-naphthylamide.**—During the interaction of chloroacetyl-β-naphthylamine with sodium arsanilate in the presence of sodium iodide the sparingly soluble chloro compound was gradually replaced by the reaction product, so that complete solution never occurred. After 4 hours' heating the mixture was diluted with water and treated with ammonia until definitely alkaline. The filtrate was warmed and treated with acetic acid, causing the precipitation of the arsonic acid as a crystalline powder. The yield from 4.4 g. of chloro compound was 5 g. For purification it was redissolved in dil. ammonia and reprecipitated with acetic acid, forming aggregates of microscopic needles which are practically insoluble in boiling water or 50% alcohol. When rapidly heated it decomposes at 285–6° to a red liquid.

Subs., 0.2154: (Kjeldahl), 10.6 cc. 0.1 *N* HCl.
Calc. for $C_{18}H_{17}O_4N_2As$: N, 7.00. Found: 6.90.

Sodium Salt.—When the acid is dissolved in warm, dil. sodium hydroxide solution and carefully neutralized with acetic acid the sparingly soluble sodium salt quickly separates as a lustrous, crystalline mass. Recrystallized from a small volume of 50% alcohol it forms aggregates of flat needles which contain approximately 4.5 molecules of water of crystallization.

Subs., air-dry, 0.8419: Loss, 0.1338 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{18}H_{16}O_4N_2AsNa.4.5H_2O$: H_2O, 16.11. Found: 15.89.
Subs., anhydrous, 0.3273: (Kjeldahl), 15.55 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1214.
Calc. for $C_{18}H_{16}O_4N_2AsNa$: N, 6.64; As, 17.74. Found: N, 6.66; As, 17.90.

N-**(Phenyl-4-arsonic Acid)-glycinediphenylamide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CON(C_6H_5)_2$.—On boiling equivalent amounts of sodium arsanilate, chloroacetyldiphenylamine,[1] and sodium iodide in 50% alcohol as in previous examples, an oily reaction product separated after several minutes. On continued boiling this redissolved and after about an hour the crystalline arsonic acid was deposited. The isolated product was dissolved in dil. ammonia, leaving an insoluble residue which was collected with boneblack and filtered off. On acidifying the filtrate to congo red with hydrochloric acid the diphenylamide was obtained and for final purification was redissolved in hot, very dil. ammonia and precipitated with acetic acid. The arsonic acid separated as long, thin, microscopic

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[1] H. Frerichs, *Chem. Zentr.*, **74**, 103–4 (1903).

leaflets which contained one molecule of water of crystallization. The anhydrous substance decomposes at 271–2° with slight preliminary softening and is very sparingly soluble in boiling water or 50% alcohol.

Subs., air-dry, 0.6797: Loss, 0.0267 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{20}H_{19}O_4N_2As.H_2O$: H_2O, 4.06. Found: 3.93.
Subs., anhydrous, 0.1780: (Kjeldahl), 8.3 cc. 0.1 *N* HCl. Subs., 0.2355: $Mg_2As_2O_7$, 0.0853.
Calc. for $C_{20}H_{19}O_4N_2As$: N, 6.57; As, 17.58. Found: N, 6.53; As, 17.48.

N-(**Phenyl-4-arsonic Acid)-glycine-4′-chloroanilide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4Cl$(*p*-).—Precipitated from the hot solution of its sodium salt with acetic acid, the substance obtained from chloroacetyl-*p*-chloroaniline quickly separates as toothed, microscopic leaflets which are often cross-shaped. It does not melt below 280° and is almost insoluble in boiling water or 50% alcohol. The sodium salt is easily salted out from its solutions by sodium acetate.

Subs., 0.3058: (Kjeldahl), 15.5 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1238.
Calc. for $C_{14}H_{14}O_4N_2ClAs$: N, 7.29; As, 19.49. Found: N, 7.10; As, 19.54.

N-(**Phenyl-4-arsonic Acid)glycine-4′-iodoanilide.**—(From chloroacetyl-*p*-iodoaniline.[1]) When added to the hot solution of its sodium salt, acetic acid causes the separation of the arsonic acid as broad, minute needles which do not melt below 275° and are practically insoluble in boiling water.

Subs., 0.2066: (Kjeldahl), 8.45 cc. 0.1 *N* HCl.
Calc. for $C_{14}H_{14}O_4N_2IAs$: N, 5.89. Found: 5.73.

Sodium Salt.—When an aqueous suspension of the acid was neutralized with sodium hydroxide and treated with sodium acetate solution the sodium salt crystallized as glistening leaflets. Recrystallized from 85% alcohol the salt separated in rosets of needles which contained 3.5 molecules of water of crystallization.

Subs., air-dry, 0.4029: Loss, 0.0448 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{13}O_4N_2IAsNa.3.5H_2O$: H_2O, 11.23. Found: 11.12.
Subs., anhydrous, 0.2946: (Kjeldahl), 11.65 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.0922.
Calc. for $C_{14}H_{13}O_4N_2IAsNa$: N, 5.63; As, 15.05. Found: N, 5.54; As, 15.11.

N-(**Phenyl-4-arsonic Acid)-glycine-4′-nitroanilide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4NO_2$(*p*-).—In this case the sparingly soluble chloroacetyl-*p*-nitraniline[2] was gradually replaced by the reaction product. The crude substance was suspended in a large volume of hot water and treated with a slight excess of ammonia. The hot, filtered solution was then treated with an excess of hydrochloric acid, causing the precipitation of the arsonic acid as long, thin, faintly yellow needles. Acetic acid is not a sufficiently strong acid completely to displace the nitro acid from its ammonium salt, and as this is also sparingly soluble in water it con-

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[1] THIS JOURNAL, 39, 1441 (1917).

[2] *J. Biol. Chem.*, 21, 112 (1915).

taminates the free arsonic acid unless a mineral acid is used as precipitant. The yield from 14.5 g. of chloroacetyl-*p*-nitraniline was 18.5 g. The arsonic acid is practically insoluble in boiling water or 50% alcohol and does not melt below 285°.

Subs., 0.1217: 11.25 cc. N (27.0°, 762 mm.). Subs., 0.3110: $Mg_2As_2O_7$, 0.1212.
Calc. for $C_{14}H_{14}O_6N_3As$: N, 10.63; As, 18.98. Found: N, 10.55; As, 18.81.

***N*-(Phenyl-4-arsonic Acid)-glycine-4′-aminoanilide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4NH_2$(*p*-).—This substance could not be made directly from *p*-amino-chloroacetanilide because of the inaccessibility of the latter compound. It is also probable that the presence of the amino group would prevent a smooth reaction in the desired sense. The substance was therefore obtained indirectly, both by the saponification of the acetyl compound described below and by reduction[1] of the nitro compound just mentioned. From the standpoint of yield the latter method is to be preferred. The former, however, is more rapid.

16 g. of (phenyl-4-arsonic acid)-glycine-4′-nitroanilide were dissolved in 50 cc. of hot 2 *N* sodium hydroxide solution, whereupon the sodium salt suddenly separated in finely divided form. This suspension was added to a bottle containing a slime of ferrous hydroxide prepared by precipitating a cold, saturated solution of 80 g. of ferrous sulfate with sufficient 25% sodium hydroxide solution to render the mixture strongly alkaline to litmus after thorough shaking. The reduction occurred at once in the cold, as evidenced by the change in color of the iron hydroxide. The bottle was immediately stoppered and shaken vigorously for several minutes and the mixture then poured on to a large suction funnel. On acidifying the filtrate with acetic acid a copious precipitate of the crude amino acid separated. This was filtered off, redissolved in hot, dil. ammonia, and reprecipitated with acetic acid. For final purification it was dissolved in a considerable volume of warm, 10% sulfuric acid, treated with bone black, and sodium acetate solution added to the warm filtrate until it no longer turned congo red paper blue. The amino acid separated in almost quantitative yield as colorless, microscopic needles or platelets. When heated rapidly it decomposes at 253–4° with preliminary darkening. It is practically insoluble in boiling water or 50% alcohol and dissolves in dil. hydrochloric acid, the hydrochloride being readily salted out by an excess of the acid. The acid solution is readily diazotized, coupling with R-salt to form a red dye.

Subs., 0.1345: 13.25 cc. N (24.5°, 760 mm.). Subs., 0.1553: $Mg_2As_2O_7$, 0.0654.
Calc. for $C_{14}H_{16}O_4N_3As$: N, 11.51; As, 20.52. Found: N, 11.31; As, 20.32.

Owing to the comparative stability of the anilide linking in *N*-(phenyl-4-arsonic acid)-glycine-4′-acetamino-anilide (see below), it was possible to remove the acetyl group in this compound by short boiling with hydro-

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[1] THIS JOURNAL, 40, 1580 (1918).

chloric acid. A partial rupture of the anilide linking could not be avoided, however, and consequently a good yield of the amino compound was not obtained. The mechanical difficulties arising from the sparing solubilities of the hydrochlorides of both the acetamino and amino acids were overcome by the addition of alcohol to the hydrolysis mixture, and the following conditions were found to permit of a rapid and smooth reaction.

5 g. of *N*-(phenyl-4-arsonic acid)-glycine-4′-acetaminoanilide were suspended in a mixture of 45 cc. of 1 : 1 hydrochloric acid and 15 cc. of alcohol. On boiling the solution under a reflux condenser the arsonic acid gradually dissolved. After 10 minutes' boiling the clear solution was chilled, causing the precipitation of the hydrochloride of the aminoanilide. The mixture was diluted with water, treated with ammonia in slight excess, heated on the water bath, and acidified with acetic acid, the amino compound separating as minute microscopic needles agreeing in all properties with the substance obtained by the reduction of the nitro compound. The yield was 2 g.

Subs., 0.1539: 15.6 cc. N (22.0°, 760 mm.). Subs., 0.2902: $Mg_2As_2O_7$, 0.1222.

Calc. for $C_{14}H_{16}O_4N_3As$: N, 11.51; As, 20.52. Found: N, 11.73; As, 20.30.

***N*-(Phenyl-4-arsonic Acid)-glycine-4′-acetaminoanilide.**—Owing to the sparing solubility of *p*-chloroacetylamino-acetanilide[1] the reaction mixture remained a thick paste in this case. After 4 hours' heating, however, the suspended material was changed in appearance and finally became completely soluble in dil. sodium hydroxide solution. The substance was purified in the usual manner. From hot, dilute solutions of the sodium salt acetic acid causes the gradual separation of the acid as aggregates of microscopic needles which are practically insoluble in boiling water or 50% alcohol and do not melt below 285°. 22 g. of arsanilic acid yielded 29 g. of the new arsonic acid.

Subs., 0.1439: 13.0 cc. N (22.5°, 763 mm.).

Calc. for $C_{16}H_{18}O_5N_3As$: N, 10.32. Found: 10.48.

Sodium Salt.—On dissolving the arsonic acid in sodium hydroxide solution to a slight alkaline reaction and adding alcohol until crystallization begins, the salt gradually separates as minute, lustrous platelets which slowly lose part of their water of crystallization on exposure to the air. A portion recrystallized from hot water and air-dried also gave uncertain figures for water of crystallization.

Subs., air-dry, 0.4421: Loss, 0.0379 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{17}O_5N_3AsNa.2H_2O$: $2H_2O$, 7.75; $2^1/_2$ H_2O, 9.49. Found: 8.57.

Subs., anhydrous, 0.1324: 11.4 cc. N (21.5°, 761 mm.). Subs., 0.3218: $Mg_2As_2O_7$, 0.1140.

Calc. for $C_{16}H_{17}O_5N_3AsNa$: N, 9.79; As, 17.47. Found: N, 9.99; As, 17.09.

***N*-(Phenyl-4-arsonic Acid)-glycine-4′-uramino-anilide,** *p*-$H_2O_3AsC_6H_4$-

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[1] THIS JOURNAL, 39, 1455 (1917).

$NHCH_2CONHC_6H_4NHCONH_2$(*p*′-).—(From *p*-chloroacetylamino-phenyl urea.[1]) After one hour's boiling the arsonic acid suddenly separated from the clear solution. After an additional hour's heating the substance was filtered off and purified over the sodium salt described below. The free acid was precipitated by acetic acid from a hot solution of the salt as pale brown, microcrystalline aggregates which contain $^1/_2$ molecule of water of crystallization. It is very sparingly soluble in boiling water, 50% alcohol, or methyl alcohol. When rapidly heated the anhydrous substance darkens above 200° and decomposes at 230°.

Subs., air-dry, 1.1959: Loss, 0.0299 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{17}O_5N_4As.0.5H_2O$: H_2O, 2.16. Found: 2.50.
Subs., anhydrous, 0.1555: 19.0 cc. N (27.0°, 759 mm.).
Calc. for $C_{15}H_{17}O_5N_4As$: N, 13.73. Found: 13.89.

Sodium Salt.—A neutral solution of the crude acid as obtained above in a small volume of dil. sodium hydroxide solution was treated with an equal volume of saturated sodium acetate solution. On standing in the refrigerator the salt crystallized as a thick mass of colorless microscopic needles. These were filtered off, washed with 85% alcohol, and recrystallized by dissolving in a small volume of warm water and treating the solution with an equal volume of alcohol. The filtered product was washed with 50% alcohol. Starting with 22 g. of arsanilic acid the yield was 24 g. The salt contains 4 molecules of water of crystallization.

Subs., air-dry, 0.5620: Loss, 0.0822 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{16}O_5N_4AsNa.4H_2O$: H_2O, 14.35. Found: 14.63.
Subs., anhydrous, 0.1311: 14.8 cc. N (20.5°, 756 mm.). Subs., 0.3050: $Mg_2As_2O_7$, 0.1087.
Calc. for $C_{15}H_{16}O_5N_4AsNa$: N, 13.02; As, 17.42. Found: N, 13.07; As, 17.20.

***N*-(Phenyl-4-arsonic Acid)-glycine-4′-methyl-5′-uramino-anilide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(CH_3)NHCONH_2$(*p*′,*m*′-). — Starting with 18.4 g. of 2-methyl-5-chloroacetylamino-phenyl urea,[2] the crude acid which separated during the heating was dissolved in dil. sodium hydroxide solution, the filtrate diluted to about 500 cc., heated, and then acidified with acetic acid. The new arsonic acid separated as aggregates of microscopic platelets and hairs which rendered filtration difficult. The yield was 22 g. The substance contains approximately $^1/_2$ molecule of water of crystallization. When rapidly heated the anhydrous acid decomposes at 257–8° with preliminary darkening and sintering and is practically insoluble in the usual solvents.

Subs., air-dry, 0.5964: Loss, 0.0103 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{19}O_5N_4As.0.5\ H_2O$: H_2O, 2.09. Found: 1.73.
Subs., anhydrous, 0.1413: 16.3 cc. N (23.0°, 758 mm.). Subs., 0.3553: $Mg_2As_2O_7$, 0.1305.
Calc. for $C_{16}H_{19}O_5N_4As$: N, 13.26; As, 17.76. Found: N, 13.27; As, 17.72.

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[1] THIS JOURNAL, **39**, 1456 (1917).

[2] *Ibid.*, **39**, 1464 (1917).

Sodium Salt.—A suspension of the acid in a little hot water was dissolved by adding just enough sodium hydroxide solution and treated with alcohol until just turbid. On rubbing and letting stand the salt slowly separated as a crystalline powder. A similar recrystallization was necessary to obtain an entirely pure product. The air-dried salt contained approximately 3.5 molecules of water of crystallization and was readily soluble in water. It can be recrystallized from hot water and is slowly salted out from strong solutions by sodium acetate.

Subs., air-dry, 0.7448: Loss, 0.0898 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{18}O_5N_4AsNa.3.5H_2O$: H_2O, 12.48. Found: 12.05.
Subs., anhydrous, 0.1518: 16.4 cc. N (21.5°, 768 mm.). Subs., 0.3272: $Mg_2As_2O_7$, 0.1174.
Calc. for $C_{16}H_{18}O_5N_4AsNa$: N, 12.61; As, 16.88. Found: N, 12.66; As, 17.31.

N-**(Phenyl-4-arsonic Acid)-glycine-3′-oxamylaminoaniline,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4NHCOCONH_2$(*m*′-).—5.2 g. of *m*-chloroacetylamino-oxanilamide[1] were boiled 6 hours with the usual reaction mixture. The precipitate was then filtered off, suspended in about a liter of water and treated with a slight excess of ammonia. The insoluble material was collected by adding boneblack and the filtrate heated nearly to boiling. The addition of acetic acid caused the gradual deposition of the arsonic acid as slightly purplish, microcrystalline aggregates. The yield was 4.4 g. The acid is almost insoluble in boiling water and very sparingly soluble in boiling 50% alcohol. When rapidly heated it gradually darkens and partly decomposes, but does not melt up to 280°.

Subs., 0.1514: 17.0 cc. N (23.0°, 757 mm.). Subs., 0.2985: $Mg_2As_2O_7$, 0.1076.
Calc. for $C_{16}H_{17}O_6N_4As$: N, 12.85; As, 17.19. Found: N, 12.90; As, 17.39.

N-**(Phenyl-4-arsonic Acid)-glycine-4′-oxamylaminoanilide.**—Owing to the insolubility of *p*-chloroacetylamino-oxanilamide[2] the heating in this case was continued for about 7 hours, in spite of which the reaction was very incomplete. The filtered solid was susepnded in a large volume of water and the mixture treated with a slight excess of ammonia. After thorough disintegration of the insoluble residue the mixture was filtered and the solution acidified with acetic acid, causing the immediate precipitation of the arsonic acid as arborescent aggregates of microscopic needles. The yield from 4.8 g. of chloro compound was only 1.1 g. The substance is practically insoluble in all neutral solvents and does not melt below 280°.

Subs., 0.1812: 20.0 cc. N (20.5°, 755 mm.). Subs., 0.2847: $Mg_2As_2O_7$, 0.1002.
Calc. for $C_{16}H_{17}O_6N_4As$: N, 12.85; As, 17.19. Found: N, 12.75; As, 16.99.

N-**(Phenyl-4-arsonic Acid)glycyl-2-aminophenol, (*N*-(Phenyl-4-arsonic Acid)-glycine-2′-hydroxyanilide),** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OH$(*o*-).—The halogen in the chloroacetylamino-phenols is extremely labile,

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[1] THIS JOURNAL, **39**, 1452 (1917).

[2] *Ibid.*, **39**, 1461 (1917).

so that these substances react with the amino group so readily as to render unnecessary the addition of sodium iodide as in the previously described syntheses. In the case of *o*-chloroacetylamino-phenol this reactivity causes a complication, since in the presence of alkalies or the sodium salts of weak acids it readily undergoes *ortho* condensation with the formation of *o*-amino-phenoxyacetic anhydride.[1] This reaction consequently paralleled the glycine formation, but in spite of this the desired arsonic acid was obtained, although in rather poor yield.

4.4 g. of arsanilic acid were dissolved in 20 cc. of *N* sodium hydroxide solution and boiled under an air-condenser with 3.8 g. of *o*-chloroacetylamino-phenol[2] for one hour, the oil which first formed gradually disappearing. On cooling the reaction product separated as an oil, but on acidifying to congo red with hydrochloric acid and scratching, it solidified almost completely. The product was collected and digested with dil. ammonia, leaving 1.5 g. of a crystalline residue, which, both by melting point (170–5°) and analysis, was shown to be *o*-amino-phenoxyacetic anhydride. On warming the ammoniacal filtrate from this by-product and acidifying slightly with hydrochloric acid, 1.7 g. of the new arsonic acid separated on cooling as lustrous crystals. When rapidly heated the substance melts and decomposes at 190° with preliminary darkening. It is soluble in cold 95% alcohol and is also easily soluble in boiling water, from which it separates on cooling as long, narrow, glistening leaflets. An alkaline solution couples readily with diazotized sulfanilic acid, yielding an orange colored solution.

Subs., 0.1496: (Kjeldahl), 8.23 cc. 0.1 *N* HCl. Subs., 0.2221: $Mg_2As_2O_7$, 0.0958,
Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48. Found: N, 7.70; As, 20.82.

A better yield of the arsonic acid was obtained by using two molecules of arsanilic acid instead of one molecule of sodium arsanilate. In this case longer boiling was necessary. 21 g. of *o*-chloroacetylamino-phenol and 50 g. of arsanilic acid (2 mols.) in 220 cc. of water were boiled under a reflux condenser for 4 hours. A clear solution was quickly obtained but this gradually darkened. At the end 50 cc. of 10% hydrochloric acid were added and on cooling and scratching the arsonic acid gradually crystallized. After purification as described above it agreed in all its properties with the product isolated by the first method. The yield was 17 g.

Subs., 0.1545: (Kjeldahl), 8.6 cc. 0.1 *N* HCl. Subs., 0.3010: $Mg_2As_2O_7$, 0.1254.
Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48. Found: N, 7.76; As, 20.11.

***N*-(Phenyl-4-arsonic Acid)glycyl-3-aminophenol (*N*-(Phenyl-4-arsonic Acid)-glycine-*m*′-hydroxyanilide).**—Owing to the special importance of this substance as the starting material for the preparation of arseno-

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[1] Aschan, *Ber.*, 20, 1524 (1887).

[2] This Journal, 41, 458 (1919).

phenylglycine-bis-*m*′-hydroxyanilide, it will be published in connection with this arseno compound in another place.

***N*-(Phenyl-4-arsonic Acid)-glycine-2′-methyl-5′-hydroxyanilide.**—When a solution of 12.4 g. of arsanilic acid in 57 cc. of *N* aqueous sodium hydroxide was boiled with 11.3 g. of 4-methyl-5-chloroacetylamino-phenol[1] a clear solution was obtained in a few minutes and deposition of the new arsonic acid began in about 20 minutes. Heating was continued on the water bath for a total of one hour, and after letting cool, the mixture was acidified to congo red with hydrochloric acid and filtered. The crude product was suspended in water, made just alkaline with sodium carbonate, and treated with boneblack after neutralizing with acetic acid. The filtrate, heated almost to the boiling point and treated with acetic acid, soon deposited the arsonic acid as glistening, pink platelets and microscopic prisms. The yield was 9.0 g., decomposing at about 220–5°, with preliminary darkening. It is very sparingly soluble in boiling water, alcohol, methyl alcohol, or acetic acid. In alkaline solution it couples with diazotized sulfanilic acid yielding a redder color than do similar compounds in which the position *para* to the hydroxy group is unoccupied.

Subs., 0.1308: (Kjeldahl), 7.0 cc. 0.1 *N* HCl. Subs., 0.3134: $Mg_2As_2O_7$, 0.1267.
Calc. for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.72. Found: N, 7.50; As, 19.49.

***N*-(Phenyl-4-arsonic Acid)-glycine-4′-methyl-5′-hydroxyanilide.**—The product from 20 g. of 2-methyl-5-chloroacetylamino-phenol[1] was worked up as in the case of the preceding compound, but as the analysis showed it to be impure it was converted into the sodium salt. The salt obtained by the addition of several volumes of alcohol to the neutral solution of the acid in sodium hydroxide solution was washed with 85% alcohol, and converted into the acid by precipitating from hot water with acetic acid. The arsonic acid forms prisms and branched leaflets which are very sparingly soluble in the usual solvents. The yield was 10.6 g. When rapidly heated to 255°, then slowly, the substance gradually darkens and softens, melting at 258° with decomposition. In alkaline solution it couples readily with diazotized sulfanilic acid.

Subs., 0.1596: (Kjeldahl), 12.1 cc. 0.1 *N* HCl. Subs., 0.3030: $Mg_2As_2O_7$, 0.1228.
Calc. for $C_{15}H_{17}O_5N_2As$: N, 7.37; As 19.72. Found: N, 7.58; As, 19.57.

***N*-(Phenyl-4-arsonic Acid)glycyl-4′-aminophenol, (*N*-(Phenyl-4-arsonic Acid)-glycine-4′-hydroxyanilide).**—After about 15 minutes the mixture (from 33 g. of arsanilic acid and 28 g. of *p*-chloroacetylamino-phenol[2]) set to an almost solid mass of lustrous crystals and the heating was continued for 45 minutes longer on the water bath. The somewhat colored product was suspended in a moderate volume of hot water and completely dissolved by the addition of dil. sodium hydroxide solution. After careful

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[1] THIS JOURNAL, 41, 459 (1919).

[2] *Ibid.*, 39, 1442 (1917).

neutralization with acetic acid the hot solution was decolorized with boneblack and the clear, hot filtrate acidified with acetic acid, yielding the pure arsonic acid as faintly pink, glistening platelets in a yield of 35 g. When rapidly heated the arsonic acid darkens and melts to a black tar at 255–60°. It is almost insoluble in boiling water, 50% alcohol, 50% acetic acid, or methyl alcohol.

Subs., 0.2673: (Kjeldahl), 14.25 cc. 0.1 *N* HCl.
Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66. Found: 7.47.

Sodium Salt.—This was readily obtained from a neutral solution of the acid in dil. sodium hydroxide on treatment with saturated sodium acetate solution. Recrystallized from hot water, the salt formed lustrous platelets which contained 4.5 molecules of water of crystallization. It is fairy easily soluble in cold water.

Subs., air-dry, 0.5730: Loss, 0.0967 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{14}O_5N_2AsNa.4.5H_2O$: H_2O, 17.26. Found: 16.87.
Subs., anhydrous, 0.3096: (Kjeldahl), 16.25 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1245.
Calc. for $C_{14}H_{14}O_5N_2AsNa$: N, 7.22; As, 19.30. Found: N, 7.36; As, 19.41.

***N*-(Phenyl-4-arsonic Acid)-glycine-*p*′-anisidide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_3$(*p*-).—This substance was readily obtained by the usual method from chloroacetyl-*p*-anisidine in the presence of sodium iodide. The arsonic acid is precipitated by acetic acid from its hot solution in dil. sodium hydroxide as lustrous leaflets which darken and soften above 230° when rapidly heated. It is practically insoluble in boiling water or boiling 50% alcohol, and gives a flesh-colored solution in conc. sulfuric acid.

Subs., 0.1575: 10.2 cc. N (23.5°, 759 mm.). Subs., 0.3422: $Mg_2As_2O_7$, 0.1368.
Calc. for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.71. Found: N, 7.45; As, 19.29.

***N*-(Phenyl-4-arsonic Acid)glycyl-1-amino-2-naphthol,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_{10}H_6OH$(1,2-).—The ease with which 1-chloroacetylamino-2-naphthol[1] reacts in the presence of alkali, alkali carbonates or salts of weak acids to form the anhydride of 1-amino-2-naphthoxyacetic acid interfered greatly with the preparation of the above arsonic acid, a fact which recalls the experience with *o*-chloroacetylamino-phenol. Of all the methods tested, the best results were given by the following procedure:

22 g. of arsanilic acid in 100 cc. of *N* sodium hydroxide solution, 20 g. of sodium iodide, 24 g. of chloroacetylamino-phenol and 100 cc. of alcohol were boiled for one hour, a large proportion of the chloroacetyl compound changing to the sparingly soluble anhydride. After dilution with water, the mixture was made ammoniacal and the insoluble anhydride (m. p. 215°) filtered off. The filtrate was acidified strongly with acetic acid and on standing in the refrigerator the arsonic acid gradually separated, contami-

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[1] THIS JOURNAL, 41, 460 (1919).

nated with unchanged arsanilic acid. The deposited substance was redissolved in dil. ammonia, treated with boneblack, and the hot filtrate acidified with hydrochloric acid, the new compound separating at once as a heavy powder consisting of aggregates of microscopic plates and prisms which contained two molecules of water of crystallization. The yield was 6.5 g. The anhydrous substance decomposes at 189–91° with preliminary darkening and softening. Although very difficultly soluble in the cold it dissolves appreciably in boiling alcohol or acetic acid. It is more easily soluble in methyl alcohol and almost insoluble in water.

Subs., air-dry, 0.5668: Loss, 0.0453 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{18}H_{17}O_5N_2As.2H_2O$: H_2O, 7.96. Found: 7.99.

Subs., anhydrous, 0.1970: (Kjeldahl), 9.55 cc. 0.1 *N* HCl. Subs., 0.3666: $Mg_2As_2O_7$, 0.1386.

Calc. for $C_{18}H_{17}O_5N_2As$: N, 6.73; As, 18.02. Found: N, 6.79; As, 18.24.

(*N*-(Phenyl-4-arsonic Acid)glycine-4′,1′-hydroxynaphthalide), *N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-1-naphthol.—4.4 g. of arsanilic acid were treated in the usual manner with 4.8 g. of 4-chloroacetylamino-1-naphthol[1] in 50% alcohol in the presence of sodium iodide for 4 hours. The deeply colored solution yielded the new arsonic acid on scratching and dilution with water. After filtration and washing with acetone in order to remove most of the color, the crude residue was dissolved in hot 20% sodium acetate solution and then treated with an equal volume of saturated sodium acetate solution. On cooling the sodium salt separated as glistening plates, and was recrystallized from a small volume of water. The yield was 4 g., containing 5.5 molecules of water of crystallization.

Subs., air-dry, 0.9469: Loss, 0.1704 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{18}H_{16}O_5N_2AsNa.5.5H_2O$: H_2O, 18.43. Found: H_2O, 17.99.

Subs., anhydrous, 0.2997: (Kjeldahl), 13.65 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1060.

Calc. for $C_{18}H_{16}O_5N_2AsNa$: N, 6.39; As, 17.11. Found: N, 6.38; As, 17.07.

On treating a hot, dilute solution of the sodium salt with acetic acid, the *free acid* separates slowly as microscopic crystals which contain approximately 1.5 molecules of water of crystallization. The anhydrous substance darkens above 200° and decomposes at 240–2°. It is practically insoluble in boiling water and but sparingly so in 50 or 95% alcohol. It is readily soluble in hot methyl alcohol.

Subs., air-dry, 0.6011: Loss, 0.0405 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{18}H_{17}O_5N_2As.1.5H_2O$: H_2O, 6.10. Found: 6.74.

Subs., anhydrous, 0.1452: 8.7 cc. N (27.5°, 760 mm.).

Calc. for $C_{18}H_{17}O_5N_2As$: N, 6.73. Found: 6.81.

***N*-(Phenyl-4-arsonic Acid)glycyl-3-amino-4,6-dichlorophenol.**—In the reaction between 2,4-dichloro-5-chloroacetylamino-phenol[2] and sodium arsanilate by the usual sodium iodide-50% alcohol method a clear solution

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[1] THIS JOURNAL, 41, 460 (1919).

[2] *Ibid.*, 41, 461 (1919).

quickly formed from which the reaction product suddenly separated. The solid was suspended in a large volume of water to prevent separation of the somewhat difficultly soluble sodium salt and dil. sodium hydroxide solution added until all but an amorphous substance had dissolved. This was collected with boneblack and the filtrate heated and acidified with acetic acid. A repetition of this process removed a further small quantity of amorphous material, 26 g. of the original chloroacetyl compound yielding 21 g. of the pure product. The new arsonic acid forms flat, colorless microscopic needles which begin to darken above 220° but melt and decompose at about 280°. It is practically insoluble in boiling water or 50% alcohol.

Subs., 0.2538: (Kjeldahl), 12.02 cc. 0.1 *N* HCl. Subs., 0.2274: $Mg_2As_2O_7$, 0.0809.
Calc. for $C_{14}H_{13}O_5N_2Cl_2As$: N, 6.44; As, 17.23. Found: N, 6.64; As, 17.16.

N-**(Phenyl-4-arsonic Acid)glycyl-3-amino-6-bromophenol.**—16.5 g. of arsanilic acid and 20 g. of 2-bromo-5-chloroacetylamino-phenol[1] yielded smoothly 23 g. of recrystallized reaction product by the sodium iodide-50% alcohol method. Acetic acid precipitates the arsonic acid from hot solutions of its salts as glistening leaflets which decompose at 255° with preliminary sintering. It is very sparingly soluble in boiling water, 50% alcohol, or methyl alcohol.

Subs., 0.1421: 7.6 cc. N (21.5°, 763 mm.).
Calc. for $C_{14}H_{14}O_5N_2BrAs$: N, 6.29. Found: 6.23.

N-**(Phenyl-4-arsonic Acid)glycyl-4-amino-pyrocatechol, (*N*-(Phenyl-4-arsonic Acid)glycine-3',4'-dihydroxyanilide).**—A solution of 33 g. of arsanilic acid in 150 cc. of *N* sodium hydroxide solution was boiled for one hour with 31 g. of 4-chloroacetylamino-pyrocatechol,[2] the reaction product partly separating from the deeply colored solution. After cooling the very dark crystalline mass was filtered off, dissolved in dil. sodium hydroxide solution and carefully neutralized with acetic acid. After treating the almost black solution with boneblack and acidifying the still deeply colored filtrate with acetic acid, the arsonic acid slowly separated as colored, microscopic leaflets. A repetition of the purification process removed most of the color, the product as finally obtained forming faintly pink, glistening leaflets. The yield was only 15 g., considerable loss having occurred during purification. When rapidly heated the substance blackens above 200° and decomposes at about 260–5°. It dissolves with difficulty in boiling water, separating on cooling as long, narrow, lustrous plates. It is very sparingly soluble in hot alcohol or methyl alcohol, more readily in hot 50% alcohol. A solution of the acid in an excess of dil. sodium hydroxide solution rapidly turns deep orange in color, while

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[1] THIS JOURNAL, 41, 464 (1919).
[2] *Ibid.*, 41, 468 (1919).

ferric chloride added to an aqueous solution of the acid causes a bluish purple coloration.

Subs., 0.1653: (Kjeldahl), 8.67 cc. 0.1 *N* HCl. Subs., 0.3105: $Mg_2As_2O_7$, 0.1274.
Calc. for $C_{14}H_{15}O_6N_2As$: N, 7.33; As, 19.61. Found: N, 7.34; As, 19.80.

***N*-(Phenyl-4-arsonic Acid)glycyl-anthranilic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CO_2H$(*o*-).—Owing to the great reactivity of the chlorine atom in chloroacetyl-anthranilic acid the reaction between this compound and sodium arsanilic did not go entirely in the desired sense, so that the yield of the complex arsonic acid was unusually poor. The most satisfactory results were obtained by the use of the ester of chloroacetyl-anthranilic acid and subsequent saponification of the resulting ester arsonic acid.

30 g. of *N*-(phenyl-4-arsonic acid)glycyl-anthranilic ethyl ester (see below) were dissolved in a definite excess of 10% sodium hydroxide solution and allowed to stand at room temperature for several hours. Heating the solution was found not only to saponify the ester group but also to cleave the amide linking with consequent formation of anthranilic acid. Acidification caused the separation of a gum which rapidly crystallized and was redissolved in hot dil. sodium acetate solution and treated hot with an excess of hydrochloric acid. The arsonic acid separated at once as characteristic octahedra. The yield was 25 g. On rapid heating it decomposes at 230–5° with preliminary softening and darkening and is practically insoluble in boiling water, but appreciably in boiling methyl or ethyl alcohol or 50% alcohol.

Subs., 0.3056: (Kjeldahl), 15.4 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1195.
Calc. for $C_{15}H_{15}O_6N_2As$: N, 7.11; As, 19.02. Found: N, 7.06; As, 18.88.

***N*-(Phenyl-4-arsonic Acid)glycyl-anthranilic Ethyl Ester,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CO_2C_2H_5$(*o*-).—25 g. of chloroacetyl-anthranilic ethyl ester,[1] in the presence of sodium iodide yielded 31 g. of crude product. Recrystallized from 50% alcohol the ester separates as rosets of delicate needles which do not decompose below 280°. It is difficultly soluble in cold methyl alcohol, more readily on heating, and also dissolves in hot 50% or 95% alcohol.

Subs., 0.1485: 8.9 cc. N (25.5°, 755 mm.).
Calc. for $C_{17}H_{19}O_6N_2As$: N, 6.64. Found: 6.81.

***N*-(Phenyl-4-arsonic Acid)-glycyl-*N*-methylanthranilic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CON(CH_3)C_6H_4CO_2H$(*o*-).—Although the reaction between sodium arsanilate and chloroacetyl-methylanthranilic acid[2] apparently proceeded partly in the desired sense, it was difficult to isolate a pure product. As in the case of the anthranilic acid compound the substance was found to be more easily prepared over the ester. For this

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[1] THIS JOURNAL, 41, 469 (1919).

[2] *Ibid.*, 41, 470 (1919).

purpose 25 g. of arsanilic acid dissolved in 115 cc. of *N* sodium hydroxide solution, 29 g. of chloroacetyl-methylanthranilic ethyl ester,[1] 22 g. of sodium iodide, and 115 cc. of alcohol were boiled under a reflux condenser for 4 hours. As attempts to obtain a crystalline reaction product failed the ester was not isolated. Instead the alcohol was allowed to boil off and the residue diluted with water. After the oil which was formed had settled, the aqueous layer was decanted and the oil again shaken with a small volume of water which was then also decanted. The crude ester so obtained was dissolved in 150 cc. of 10% sodium hydroxide solution, filtered, and allowed to stand 4 hours at room temperature. The alkaline solution was then acidified to congo red with hydrochloric acid, causing the separation of the acid as a gum which gradually solidified. This was purified by again dissolving in dil. alkali and acidifying with hydrochloric acid until faintly acid to congo red. The resulting cloudy solution gradually deposited the acid as microscopic aggregates of needles or short, flat plates. The yield was 16 g. When rapidly heated the acid darkens and decomposes at 230°. It is very difficultly soluble in boiling water or boiling methyl alcohol, but fairly readily so in hot 50% alcohol, from which it can be recrystallized.

Subs., 0.3213: (Kjeldahl), 15.7 cc. 0.1 *N* HCl. Subs., 0.3256: $Mg_2As_2O_7$, 0.1245.
Calc. for $C_{16}H_{17}O_6N_2As$: N, 6.86; As, 18.36. Found: N, 6.85; As, 18.46.

***N*-(Phenyl-4-arsonic Acid)glycyl-2-amino-benzamide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4CONH_2$(*o*-).—After boiling equivalent amounts of sodium arsanilate, *o*-chloroacetylamino-benzamide,[2] and sodium iodide for two hours in 50% alcohol a clear solution resulted. Crystallization of the reaction product was started by rubbing with a rod and the crude product purified by dissolving in dil. sodium hydroxide and adding acetic acid. In this way it crystallizes slowly as faintly yellow, radiating masses of delicate microscopic needles which contain one molecule of water of crystallization. When rapidly heated to 165° and then slowly it sinters and slowly melts down at 170°. It is sparingly soluble in cold water, alcohol or 50% alcohol, but readily soluble on warming. It is appreciably soluble in methyl alcohol in the cold.

Subs., air-dry, 0.8645: Loss, 0.0384 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{16}O_5N_3As.H_2O$: H_2O, 4.38. Found: 4.44.
Subs., anhydrous, 0.1828: (Kjeldahl), 14.05 cc. 0.1 *N* HCl.
Calc. for $C_{15}H_{16}O_5N_3As$: N, 10.69. Found: 10.76.

Sodium Salt.—The neutral solution of the acid in a small volume of dil. sodium hydroxide, was treated with several volumes of alcohol. On standing in the refrigerator the salt gradually crystallized. On recrystallization from 85% alcohol it formed globules of minute crys-

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[1] THIS JOURNAL, **41**, 470 (1918).
[2] *Ibid.*, **39**, 1442 (1917).

tals which, like the acid, had a slightly yellow color. It contains 4.5 molecules of water of crystallization and dissolves readily in water.

Subs., air-dry, 0.5076: Loss, 0.0808 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{15}H_{15}O_5N_3AsNa.4.5H_2O$: H_2O, 16.33. Found: 15.92.

Subs., anhydrous, 0.3235: (Kjeldahl), 23.65 cc. 0.1 N HCl. Subs., 0.3825: $Mg_2As_2O_7$, 0.1441.

Calc. for $C_{15}H_{15}O_5N_3AsNa$: N, 10.13; As, 18.06. Found: N, 10.24; As, 18.18.

N-**(Phenyl-4-arsonic Acid)glycyl-3-amino-benzamide.**—As in the previous case m-chloroacetylamino-benzamide[1] yielded after several hours' boiling a supersaturated solution of the reaction product which crystallized only on chilling and rubbing. On treating a solution of the crude product in dil. sodium hydroxide with acetic acid the pure arsonic acid separated as irregular, microscopic platelets. Recrystallized from hot 50% alcohol, in which it is rather sparingly soluble, it separates as rosets of microscopic spears which contain between 2 and 2.5 molecules of water of crystallization. The acid is practically insoluble in boiling water, and when rapidly heated, darkens and shows signs of decomposition above 200° but does not decompose completely until 280° is reached.

Subs., air-dry, 0.9688: Loss, 0.0891 *in vacuo* at 100° over P_2O_5.

Calc. for $C_{15}H_{16}O_5N_3As.2H_2O$: H_2O, 8.39; 2.5 H_2O, 10.27. Found: 9.20.

Subs., anhydrous, 0.2713: (Kjeldahl), 20.5 cc. 0.1 N HCl; $Mg_2As_2O_7$, 0.1075.

Calc. for $C_{15}H_{16}O_5N_3As$: N, 10.69; As, 19.07. Found: N, 10.59; As, 19.13.

N-**(Phenyl-4-arsonic Acid)-glycyl-3-aminobenzoyl-urea,** p-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_4CONHCONH_2$($m$-).—In this case the sparingly soluble m-chloroacetyl-aminobenzoyl-urea,[2] was gradually replaced by the new arsonic acid. After 4 hours' heating the resulting product was collected, suspended in water, and treated with dil. sodium carbonate solution until the solution remained slightly alkaline on thorough mixing and the arsonic acid was completely extracted from an insoluble residue. This was collected in the cold with boneblack and the clear filtrate treated with sodium acetate until the sodium salt separated. After standing in the refrigerator the salt was filtered off and washed with 20% sodium acetate solution, then with 85% alcohol. For purification it was dissolved in a small volume of water and treated with two volumes of alcohol. On scratching the sodium salt separated as thick, colorless masses of delicate microscopic hairs which contained 8 molecules of water of crystallization.

Subs., air-dry, 0.5560: Loss, 0.1323 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{16}O_6N_4AsNa.8H_2O$: H_2O, 23.93. Found: 23.80.

Subs., anhydrous, 0.1335: 14.45 cc. N (26.0°, 756 mm.). Subs., 0.2892: $Mg_2As_2O_7$, 0.0970.

Calc. for $C_{16}H_{16}O_6N_4AsNa$: N, 12.23; As, 16.36. Found: N, 12.29; As, 16.19.

On addition of acetic acid to the hot dilute solution of the salt the free

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[1] THIS JOURNAL, 39, 1442 (1917).

[2] *Ibid.*, 39, 2430 (1917).

arsonic acid separates as sheaves and plumes of microscopic needles which decompose at about 280° with preliminary darkening and sintering. It is practically insoluble in boiling water or 50% alcohol.

Subs., 0.1663: (Kjeldahl), 15.25 cc. 0.1 *N* HCl.
Calc. for $C_{16}H_{17}O_6N_4As$: N, 12.84. Found: 12.84.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-benzamide.**—The reaction in the case of *p*-chloroacetylamino-benzamide[1] occurred quickly as evidenced by the rapid disappearance of the sparingly soluble chloroacetyl compound, followed soon after by the sudden precipitation of the new arsonic acid. This was suspended in water and dissolved by the careful addition of dil. sodium hydroxide solution. After neutralization to litmus with acetic acid the solution was heated, filtered, and the filtrate treated with sodium acetate until the sodium salt began to separate. This was recrystallized from hot water, in which it is easily soluble, separating on cooling as rosets of thin, microscopic needles which contain 4.5 molecules of water of crystallization.

Subs., air-dry, 0.3410: Loss, 0.0564 *in vacuo* at 100° over P_2O_5.
Calc. for $C_{15}H_{15}O_5N_3AsNa.4.5H_2O$: H_2O, 16.33. Found: 16.54.
Subs., anhydrous, 0.3187: (Kjeldahl), 22.5 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1210.
Calc. for $C_{15}H_{15}O_5N_3AsNa$: N, 10.13; As, 18.06. Found: N, 9.89; As, 18.33.

A hot, dilute solution of the salt, treated with acetic acid, immediately deposited the insoluble *arsonic acid* as nodules of microscopic needles which do not melt below 280°.

Subs., 0.1034: 9.7 cc. N (22.0°, 757 mm.).
Calc. for $C_{15}H_{16}O_5N_3As$: N, 10.69. Found: N, 10.81.

***N*-(Phenyl-4-arsonic Acid)glycyl-5-amino-salicylamide,** *p*-$H_2O_3AsC_6H_4$-$NHCH_2CONHC_6H_3(OH)CONH_2$(*p,m*-).—42 g. of 5-chloroacetylamino-salicylamide,[2] by the sodium iodide method, after 2 hours boiling and purification of the crude product in the usual way, yielded 45 g. of the pure arsonic acid as glistening scales which contained one molecule of water of crystallization. When rapidly heated the anhydrous substance softens above 190° and gradually decomposes until fluid at about 255°. It is very sparingly soluble in boiling water or 50% alcohol, such solutions giving a brownish purple color with ferric chloride. In alkaline solution it couples with diazotized sulfanilic acid.

Subs., air-dry, 0.7932: Loss, 0.0356 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{15}H_{16}O_6N_3As.H_2O$: H_2O, 4.40. Found: H_2O, 4.49.
Subs., anhydrous, 0.3148 (Kjeldahl), 22.5 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1179.
Calc. for $C_{15}H_{16}O_6N_3As$: N, 10.27; As, 18.32. Found: N, 10.01; As, 18.08.

***N*-(Phenyl-4-arsonic Acid)-glycyl-3-amino-phenylacetamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_2CONH_2$(*m*-).—4.6 g. of *m*-chloro-

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[1] THIS JOURNAL, 39, 1443 (1917).

[2] *Ibid.*, 39, 2420 (1917).

acetylamino-phenylacetamide,[1] using sodium iodide, gave a clear solution from which the crude product separated on dilution and rubbing. The substance was redissolved in dil. ammonia and treated with acetic acid, the pure arsonic acid separating as masses of microscopic needles which darken slightly above 220° and decompose at 275–80°. It is soluble in boiling water and 50% alcohol. The yield was 5.2 g.

Subs., 0.1427 12.8 cc. N (22.0°, 764 mm.). Subs., 0.3065 $Mg_2As_2O_7$, 0.1166.
Calc. for $C_{16}H_{18}O_5N_3As$: N, 10.32; As, 18.41. Found: N, 10.44; As, 18.35.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-phenylacetic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_2CO_2H$(*p*-).—15.4 g. of arsanilic acid were dissolved in 70 cc. of *N* sodium hydroxide solution and boiled for one hour with 16 g. of *p*-chloroacetylamino-phenylacetic acid.[2] The oil which separated on cooling soon crystallized and was triturated with 70 cc. of *N* hydrochloric acid solution, filtered off, washed with water, and dried. The yield of crude product, 24 g. was dissolved in dil. sodium hydroxide solution, made faintly acid with acetic acid, treated with boneblack, and the filtrate diluted to about 500 cc., warmed on the water bath, and treated with hydrochloric acid until just acid to congo red. The arsonic acid which separated was recrystallized from 85% alcohol, separating slowly as practically colorless, microscopic globules. The dried acid gradually darkens on heating, finally melting and decomposing on keeping the bath at 280° for a few moments. The anhydrous substance is pale yellow, losing its color without dissolving when boiled with water. It is quite soluble in boiling 85% alcohol or methyl alcohol and dissolves only sparingly in boiling acetic acid.

Subs., 0.2077: (Kjeldahl), 10.25 cc. 0.1 *N* HCl. Subs., 0.2747: $Mg_2As_2O_7$, 0.1038.
Calc. for $C_{16}H_{17}O_6N_2As$: N, 6.87; As, 18.36. Found: N, 6.91; As, 18.24.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-phenylacetamide.** — (From *p*-chloroacetylamino-phenylacetamide[3] by the 50% alcohol and sodium iodide method). The crude acid was reprecipitated from its solution in hot dil. ammonia by acetic acid, separating as plumes of microscopic hairs. The arsonic acid is only sparingly soluble in boiling water or 50% alcohol and does not melt below 280°. Because of the aliphatic amide linking it is very sensitive to fixed alkali.

Subs., 0.1305: 11.6 cc. N (24.0°, 771 mm.). Subs., 0.3092: $Mg_2As_2O_7$, 0.1192.
Calc. for $C_{16}H_{18}O_5N_3As$: N, 10.32; As, 18.41. Found: N, 10.3[illegible]; As, 18.58.

Sodium Salt.—The acid was suspended in a small volume of water and very cautiously treated with dil. sodium hydroxide solution until just dissolved. The solution was then carefully neutralized to litmus with acetic acid and alcohol added until crystallization began. The salt

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[1] THIS JOURNAL, **39**, 2421 (1917).

[2] *Ibid.*, 41, 469 (1919).

[3] *Ibid.*, **39**, 1444 (1917).

separated as glistening platelets which, after air-drying, contained 2.5 molecules of water of crystallization and dissolved readily in water.

Subs., air-dry, 0.3945: Loss, 0.0371 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{17}O_5N_3AsNa.2.5H_2O$: H_2O, 9.49. Found: 9.40.

Subs., anhydrous, 0.1489: 12.8 cc. N (22.0°, 756 mm.). Subs., 0.2625: $Mg_2As_2O_7$, 0.0936.

Calc. for $C_{16}H_{17}O_5N_3AsNa$: N, 9.79; As, 17.47. Found: N, 9.91; As, 17.21.

N-**(Phenyl-4-arsonic Acid)-glycyl-4-amino-phenylacetureide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4CH_2CONHCONH_2$(*p*-). — The very sparingly soluble *p*-chloroacetylamino-phenylacetylurea,[1] was very slowly and incompletely replaced by the reaction product. After 5 hours' boiling the somewhat gelatinous mass was diluted with water and filtered, and in order to extract the desired arsonic acid completely the residue was placed in a bottle with several hundred cc. of water containing a slight excess of ammonia and the mixture shaken in a machine until thoroughly disintegrated. Boneblack was then added and the mixture again shaken in order to collect the insoluble, gelatinous material. The filtrate was heated and acidified with acetic acid, causing the separation of the crystalline arsonic acid. This was converted into the *sodium salt* by suspending in a small volume of warm water and very cautiously treating with dil. sodium hydroxide until solution was just complete and the reaction was only faintly alkaline to litmus. The filtered solution was warmed and treated with alcohol until turbid, the salt separating on cooling as microscopic, hexagonal plates which contained 3 molecules of water of crystallization. The yield was 4.7 g.

Subs., air-dry, 0.4511: Loss, 0.0483 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{17}H_{18}O_6N_4AsNa.3H_2O$: H_2O, 10.27. Found: 10.71.

Subs., anhydrous, 0.1500: 15.6 cc. N (25.0°, 758 mm.). Subs., 0.2521: $Mg_2As_2O_7$, 0.0815.

Calc. for $C_{17}H_{18}O_6N_4AsNa$: N, 11.87; As, 15.88. Found: N, 11.88; As, 15.61.

On adding acetic acid to a hot solution of the sodium salt the free *arsonic acid* separated gradually as plumes of minute hairs which are almost insoluble in boiling water or 50% alcohol. It darkens slightly, but does not melt below 280°.

Subs., 0.1538: (Kjeldahl), 13.45 cc. 0.1 *N* HCl.

Calc. for $C_{17}H_{19}O_6N_4As$: N, 12.45. Found: 12.25.

N-**(Phenyl-4-arsonic Acid)-glycyl-2-amino-phenoxyacetamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_2CONH_2$(*o*-).—The reaction product from *o*-chloroacetylamino-phenoxyacetamide,[2] was dissolved in dil. ammonia in order to avoid danger of saponification of the amide group. The addition of acetic acid to the heated filtrate caused the separation of the acid as a voluminous mass of microscopic needles which contained

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[1] THIS JOURNAL, **39**, 2434 (1917).

[2] *Ibid.*, **39**, 2422 (1917).

one molecule of water of crystallization. The yield was 10 g. The acid is very sparingly soluble in boiling water and somewhat more so in hot 50% alcohol, from which it crystallizes in minute, glistening needles on cooling. When anhydrous it decomposes at about 280° with preliminary darkening.

Subs., air-dry, 0.0845: Loss, 0.0033 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{18}O_6N_3As.H_2O$: H_2O, 4.08. Found: 3.90.

Subs., anhydrous, 0.1370: 11.95 cc. N (23.0°, 756 mm.). Subs., 0.3369: $Mg_2As_2O_7$, 0.1222.

Calc. for $C_{16}H_{18}O_6N_3As$: N, 9.93; As, 17.72. Found: N, 10.02; As, 17.50.

***N*-(Phenyl-4-arsonic Acid)-glycyl-3-amino-phenoxyacetic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_2CO_2H$(*m*-).—In this case the addition of sodium iodide as a catalyzer was unnecessary. 22 g. of arsanilic acid were dissolved in 100 cc. of *N* sodium hydroxide solution, 25 g. of *m*-chloroacetylamino-phenoxyacetic acid[1] were added and the mixture boiled for one hour. An oil separated from the clear solution on cooling. On the addition of hydrochloric acid in excess the new arsonic acid rapidly crystallized. After filtration it was dissolved in sufficient dil. sodium hydroxide solution, diluted to about 500 cc. and warmed. On adding hydrochloric acid until congo red paper turned color, a finely divided, oily suspension was formed which solidified on rubbing, forming radiating masses of microcrystals containing approximately one molecule of water of crystallization. The yield was 28 g. The acid is fairly easily soluble in boiling water or 50% alcohol. When rapidly heated the anhydrous substance softens at 180–90°, then darkens and finally decomposes at about 250–60°.

Subs., air-dry, 0.5668: Loss, 0.0197 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{16}H_{17}O_7N_2As.H_2O$: H_2O, 4.07. Found: 3.47.

Subs., anhydrous, 0.1583: (Kjeldahl), 7.53 cc. 0.1 *N* HCl. Subs., 0.3019: $Mg_2As_2O_7$, 0.1088.

Calc. for $C_{16}H_{17}O_7N_2As$: N, 6.60; As, 17.68. Found: N, 6.66; As, 17.40.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-phenoxyacetic Acid.**—This substance was obtained as in the case of the previously described *meta* isomer, from *p*-chloroacetylamino-phenoxyacetic acid.[2] After 30 minutes' boiling the clear solution suddenly set to a thick, crystalline mass, after which heating was continued 30 minutes longer on the water bath. The product was dissolved in sufficient sodium hydroxide solution, diluted to about 500 cc., heated on the water bath, and acidified to congo red with hydrochloric acid. The arsonic acid immediately separated as a colorless powder, which appeared as minute globules under the microscope. The yield was 30 g. When a hot, dilute solution of the salt (see below) is acidified with acetic acid the arsonic acid gradually separates

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[1] THIS JOURNAL, **41**, 466 (1919).

[2] *Ibid.*, **39**, 2436 (1917).

as aggregates of flat, microscopic needles and platelets. It is practically insoluble in hot alcohol, methyl alcohol, or water, but is appreciably soluble in boiling 50% alcohol. The acid darkens above 250° but does not melt below 285°.

Subs., 0.1495: (Kjeldahl), 7.05 cc. 0.1 *N* HCl.
Calc. for $C_{16}H_{17}O_7N_2As$: N, 6.61. Found: 6.59.

Sodium Salt.—On addition of alcohol to a neutral solution of the acid in dil. sodium hydroxide solution until crystallization started, the sodium salt separated as glistening, microscopic leaflets which contained 3 molecules of water of crystallization.

Subs., air-dry, 0.5258: Loss, 0.0535 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{15}O_7N_2AsNa_2.3H_2O$: H_2O, 10.34. Found: 10.18.
Subs., anhydrous, 0.1441: 7.5 cc. N (23.0°, 765 mm.). Subs., 0.3417: $Mg_2As_2O_7$, 0.1133.
Calc. for $C_{16}H_{15}O_7N_2AsNa_2$: N, 5.99; As, 16.02. Found: N, 6.05; As, 16.02.

***N*-(Phenyl-4-arsonic Acid)-glycyl-4-amino-phenoxyacetamide.**—16 g. of *p*-chloroacetylamino-phenoxyacetamide[1] were employed, using sodium iodide. The reaction product which separated during the heating was purified by dissolving in dil. ammonia and reprecipitating with acetic acid. The yield was 16.5 g. The acid separates from hot, dilute solutions of its salts on adding acetic acid as sheaves and plumes of minute, flat needles which do not melt below 280°. It is very sparingly soluble in boiling water or 50% alcohol.

Subs., 0.1433: 12.6 cc. N (22.0°, 747 mm.).
Calc. for $C_{16}H_{18}O_6N_3As$: N, 9.93. Found: 10.01.

Sodium Salt.—As the amide group is rather sensitive to fixed alkali, sodium carbonate was used to dissolve the acid suspended in a small volume of hot water. The sodium salt began to separate on cooling and was more completely precipitated by adding sodium acetate solution. Recrystallized from water it formed long, flat, microscopic needles containing 5 molecules of water of crystallization.

Subs., air-dry, 1.3832: Loss, 0.2362 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{16}H_{17}O_6N_3AsNa.5H_2O$: H_2O, 16.83. Found: 17.08.
Subs., anhydrous, 0.2846: (Kjeldahl), 19.3 cc. 0.1 *N* HCl. Subs., 0.2936: $Mg_2As_2O_7$, 0.1010.
Calc. for $C_{16}H_{17}O_6N_3AsNa$: N, 9.44; As, 16.84. Found: N, 9.50; As, 16.60.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-phenoxyacetylurea,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4OCH_2CONHCONH_2$(*p*-). — 5.8 g. of the almost insoluble *p*-chloroacetylamino-phenoxyacetylurea[2] were gradually replaced by the new arsonic acid. After 4 hours the filtered product was suspended in warm water and sodium carbonate added until the arsonic acid was completely extracted from an insoluble residue and

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[1] THIS JOURNAL, **39**, 2423 (1917).

[2] *Ibid.*, **39**, 2435, 2436 (1917).

the solution remained just alkaline to litmus. The use of sodium hydroxide was avoided owing to the lability of the ureide group. The insoluble residue was collected with boneblack and the clear filtrate salted out with sodium acetate. After standing in the refrigerator the filtered salt was washed with 20% sodium acetate solution and then 85% alcohol, and purified by dissolving in a small volume of warm water and treating with two volumes of alcohol. On cooling the *sodium salt* gradually separated as aggregates of microscopic needles containing 4 molecules of water of crystallization. The yield was 4.5 g.

Subs., air-dry, 0.3254: Loss, 0.0419 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{17}H_{18}O_7N_4AsNa.4H_2O$: H_2O, 12.86. Found: 12.88.

Subs., anhydrous, 0.1301: 13.0 cc. N (25.0°, 766 mm.). Subs., 0.1479: $Mg_2As_2O_7$, 0.0467.

Calc. for $C_{17}H_{18}O_7N_4AsNa$: N, 11.48; As, 15.36. Found: N, 11.54; As, 15.24.

On adding acetic acid to a hot, dilute solution of the salt the *arsonic acid* separated as rosets of microscopic needles which contained $^1/_2$ molecule of water of crystallization. The anhydrous acid slowly decomposes at about 290° with preliminary darkening, and is very difficultly soluble in boiling water or 50% alcohol.

Subs., air-dry, 0.4852: Loss, 0.0071 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{17}H_{19}O_7N_4As.0.5H_2O$: H_2O, 1.89. Found: 1.46.

Subs., anhydrous, 0.1580: (Kjeldahl), 13.45 cc. 0.1 *N* HCl.

Calc. for $C_{17}H_{19}O_7N_4As$: N, 12.02. Found: 11.92.

***N*-(Phenyl-4-arsonic Acid)glycyl-3-methyl-4-amino-phenoxyacetic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(CH_3)OCH_2CO_2H$(*o,p*-).—4.4 g. of arsanilic acid, dissolved in 20 cc. of *N* sodium hydroxide solution, and 5.2 g. of 3-methyl-4-chloroacetylamino-phenoxyacetic acid[1] yielded a clear solution on boiling. On chilling after one hour an oil separated and slowly crystallized. A solution of the crude substance in dil. sodium hydroxide was warmed and acidified with hydrochloric acid to congo red, after which the small amount of flocculent precipitate carrying coloring matter was rapidly filtered off. On cooling and standing 3 g. of the arsonic acid slowly separated as a crust on the sides of the vessel. For analysis it was recrystallized from a small volume of 50% alcohol. As so obtained the substance decomposes from 250–260° with preliminary sintering. The acid is difficult to obtain in well-defined crystals as it easily forms supersaturated solutions, crystallizes very slowly, and separates as a gum when rapidly thrown out of solution. When a dilute solution of the sodium salt described below is acidified with acetic acid the substance separates very gradually as warty aggregates of microscopic needles which decompose at 270° with preliminary darkening. It is appreciably soluble in methyl alcohol and in boiling water and readily in hot methyl or ethyl alcohol.

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[1] THIS JOURNAL, 39, 2201 (1917).

Subs., 0.2008: (Kjeldahl), 9.08 cc. 0.1 *N* HCl. Subs., 0.1802: $Mg_2As_2O_7$, 0.0660.
Calc. for $C_{17}H_{19}O_7N_2As$: N, 6.39; As, 17.12. Found: N, 6.33; As, 17.68.

Sodium Salt.—When a hot, neutral solution of the acid in a small volume of sodium hydroxide solution was treated with alcohol it yielded an oil which gradually crystallized on cooling and standing, while well-defined needles slowly separated from the supernatant liquor. The salt obtained in this way contained water of crystallization but the amount was not determined. It is easily soluble in water.

Subs., anhydrous, 0.3198: (Kjeldahl), 13.45 cc. 0.1 *N* HCl; $Mg_2As_2O_7$, 0.1040.
Calc. for $C_{17}H_{18}O_7N_2AsNa_2$: N, 5.81; As, 15.54. Found: N, 5.89; As, 15.69.

***N*-(Phenyl-4-arsonic Acid)glycyl-3-amino-benzenesulfonamide,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4SO_2NH_2$(*m*-).—Equivalent amounts of sodium arsanilate, *m*-chloroacetylamino-benzenesulfonamide,[1] and sodium iodide in 50% alcohol yielded a clear solution after several hours' boiling, from which the reaction product crystallized on cooling and rubbing. The collected product, after solution in dil. ammonia, was precipitated by acetic acid as flat, glistening, microscopic needles, often grouped in rosets. 21.5 g. of the chloroacetyl compound yielded 25 g. of the arsonic acid. It decomposes at about 265° with preliminary darkening and is difficultly soluble in boiling water or 50% alcohol.

Subs., 0.1755: 15 cc. N (23.0°, 756 mm.).
Calc. for $C_{14}H_{16}O_6N_3SAs$: N, 9.79. Found: 9.81.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-benzenesulfonic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4SO_3H$(*p*-).—16.5 g. of arsanilic acid were dissolved in 75 cc. of *N* sodium hydroxide solution and 25 g. of sodium chloroacetyl-sulfanilate[2] were added. After boiling the mixture for 30 minutes and cooling, the resulting clear solution was treated with an excess of hydrochloric acid. The arsonic acid separated on rubbing and was filtered off and washed with 10% hydrochloric acid. Reprecipitated from solution in dil. ammonia with hydrochloric acid, the pure arsonic acid separated slowly as flat, lustrous needles. The yield was 20 g. The acid is appreciably soluble in cold water, but less so in 10% hydrochloric acid solution. It is readily soluble in hot water, from which it separates on cooling as aggregates of minute, flat needles which contain two molecules of water of crystallization. It is sparingly soluble in alcohol and practically insoluble in acetone. The anhydrous substance slowly softens and decomposes at 245–6°.

Subs., air-dry, 0.8815: Loss, 0.0683 *in vacuo* at 100° over H_2SO_4.
Calc. for $C_{14}H_{15}O_7N_2SAs.2H_2O$: H_2O, 7.73. Found: 7.75.
Subs., anhydrous, 0.1537: (Kjeldahl), 7.14 cc. 0.1 *N* HCl. Subs., 0.3036: $Mg_2As_2O_7$, 0.1076.
Calc. for $C_{14}H_{15}O_7N_2SAs$: N, 6.51; As, 17.42. Found: N, 6.50; As, 17.11.

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[1] THIS JOURNAL, 39, 2429 (1917).

[2] *Ibid.*, 41, 470 (1919).

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-benzenesulfonamide.**—The product from 21.5 g. of *p*-chloroacetylamino-benzenesulfonamide[1] in the presence of sodium iodide, was dissolved in dil. ammonia. On acidification of the hot, dilute solution with acetic acid the new arsonic acid rapidly separated as colorless aggregates of thin, microscopic leaflets and needles. The yield was 30 g. The acid is insoluble in boiling water or 50% alcohol, and on rapid heating sinters slightly, but does not melt below 280°.

Subs., 0.1374: 11.6 cc. N (20.0°, 769 mm.). Subs., 0.3019: $Mg_2As_2O_7$, 0.1078.

Calc. for $C_{14}H_{16}O_6N_3SAs$: N, 9.79; As, 17.45. Found: N, 9.95; As, 17.23.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-6-hydroxybenzenesulfonic Acid,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_3(OH)SO_3H$(*m,p*-).—22 g. of arsanilic acid in 100 cc. of *N* sodium hydroxide solution and 30 g. of the sodium salt of 4-chloroacetylamino-6-hydroxybenzenesulfonic acid[2] were boiled for 30 minutes and the clear solution then chilled and treated with 25 cc. of conc. hydrochloric acid. On scratching and standing in the refrigerator the reaction product crystallized and was filtered off and washed with 10% hydrochloric acid. The crude substance was suspended in water, treated with sodium acetate solution until completely dissolved, warmed, and the solution then treated with conc. hydrochloric acid until a concentration of about 10% hydrochloric acid was reached. On cooling the arsonic acid slowly separated as a thick crust of crystals which was washed with 10% hydrochloric acid and then with ice water. The yield was 25 g. The acid separates with approximately 1.5 molecules of water of crystallization and is fairly readily soluble in water at ordinary temperatures, but like many sulfonic acids it is less soluble in dil. hydrochloric acid. It separates from hot water on thorough chilling as microscopic leaflets and is difficultly soluble in hot alcohol, methyl alcohol or acetic acid. In alkaline solution it couples readily with diazotized sulfanilic acid. The anhydrous substance softens and darkens above 200°, but does not melt below 275°.

Subs., air-dry, 0.7833: Loss, 0.0488 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{14}H_{15}O_8N_2SAs.1.5H_2O$: H_2O, 5.71. Found: 6.23.

Subs., anhydrous, 0.2022: (Kjeldahl), 9.25 cc. 0.1 *N* HCl. Subs., 0.2258: $Mg_2As_2O_7$, 0.0798.

Calc. for $C_{14}H_{15}O_8N_2SAs$: N, 6.28; As, 16.81. Found: N, 6.40; As, 17.06.

***N*-(Phenyl-4-arsonic Acid)glycyl-4-amino-acetophenone,** *p*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_4COCH_3$(*p*-).—4.3 g. of *p*-chloroacetylamino-acetophenone[3] with sodium iodide yielded 4 g. of the crystalline arsonic acid, after purification in the usual manner. The acid separates from hot, dilute solutions of its salts on addition of acetic acid as long, fine hairs

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[1] THIS JOURNAL, **39**, 2429 (1917).

[2] *Ibid.*, **41**, 471 (1919).

[3] *Ibid.*, **41**, 469 (1919).

which do not melt below 280°. It is almost insoluble in boiling water and but sparingly so in hot 50% alcohol. It dissolves in conc. sulfuric acid with a yellow color.

Subs., 0.1538: 9.6 cc. N (25.5°, 768 mm.). Subs., 0.3164: $Mg_2As_2O_7$, 0.1240.

Calc. for $C_{16}H_{17}O_6N_2As$: N, 7.15; As, 19.10. Found: N, 7.22; As, 18.91.

(B) Derivatives of *o*-Arsanilic acid.

***N*-(Phenyl-2-arsonic Acid)glycineanilide** *o*-$H_2O_3AsC_6H_4NHCH_2CONHC_6H_5$.—This substance was prepared in the same way as the *p*-derivative from *o*-arsanilic acid[1] and chloroacetanilide. The arsonic acid separated slowly on standing, and precipitation was completed by diluting the reaction mixture. The crude product was ground up with dil. hydrochloric acid and recrystallized from 50% alcohol, crystallizing on seeding as radiating masses of minute prisms with one molecule of water of crystallization. The yield equaled the amount of *o*-arsanilic acid used. The anhydrous substance softens at 158°, melts at 160–3° with slow gas evolution, and dissolves very easily in boiling 50% alcohol, although sparingly in the cold. It is very difficultly soluble in boiling water and also in cold acetic acid, but dissolves readily in the latter on warming. It is also easily soluble in cold methyl alcohol, less readily in ethyl alcohol.

Subs., air-dry, 0.6579: Loss, 0.0363 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{14}H_{15}O_4N_2As.H_2O$: H_2O, 4.89. Found: 5.52.

Subs., anhydrous, 0.2171: (Kjeldahl), 12.25 cc. 0.1 *N* HCl. Subs., 0.3047: $Mg_2As_2O_7$, 0.1364.

Calc. for $C_{14}H_{15}O_4N_2As$: N, 8.00; As, 21.39. Found: N, 7.91; As, 21.60.

***N*-(Phenyl-2-arsonic Acid)glycyl-2-aminophenol.**—22 g. of *o*-arsanilic acid and 19 g. of *o*-chloroacetylamino-phenol in 200 cc. of 0.5 *N* sodium hydroxide solution were boiled for 1/2 hour. On cooling the clear solution deposited an oil, part of which dissolved on rendering the mixture ammoniacal, leaving a copious residue of *o*-amino-phenoxyacetic anhydride.[2] On acidifying the filtrate with hydrochloric acid the oil which first separated was soon followed by crystals, and on standing in the ice-box the entire product crystallized. The crude substance was dissolved in dil. ammonia and the solution then acidified faintly with acetic acid and treated with boneblack. On adding hydrochloric acid carefully to the hot filtrate until just acid to congo red the arsonic acid separated as beautiful balls of glistening needles which soon filled the liquid. The yield was 8 g., containing 0.5 molecule of water of crystallization. When anhydrous it melts and decomposes at 151–3°. From hot water, in which it is but sparingly soluble, it separates on cooling as long, silky needles. It is fairly readily soluble in cold alcohol or methyl alcohol and easily

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[1] THIS JOURNAL, 40, 1583 (1918).

[2] Cf. the *p*-arsonic acid, p. 1621.

so in hot 50% alcohol. An alkaline solution couples readily with diazotize sulfanilic acid.

Subs., air-dry, 0.7450: Loss, 0.0197 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{14}H_{15}O_5N_2As.0.5H_2O$: H_2O, 2.40. Found: 2.64.

Subs., anhydrous, 0.2520: (Kjeldahl), 14.0 cc. 0.1 *N* HCl. Subs., 0.2734: $Mg_2As_2O_7$, 0.1178.

Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48. Found: N, 7.78; As, 20.79.

***N*-(Phenyl-2-arsonic Acid)glycyl-3-aminophenol.**—22 g. of *o*-arsanilic acid dissolved in 100 cc. of *N* sodium hydroxide solution and 19 g. of *m*-chloroacetylamino-phenol[1] were boiled for 30 minutes. On cooling a deep red oil separated, but on adding hydrochloric acid until acid to congo red, it crystallized on rubbing. The substance was then filtered off, washed with water, suspended in a small volume of water, and dissolved by the addition of ammonia. On rendering slightly acid with acetic acid the deep colored solution deposited a dark, gummy precipitate which was collected in the cold with boneblack and filtered. The filtrate was then heated with boneblack, which removed most of the color. A pink color still persisted in the filtrate, a property which all of the substances derived from *m*-chloroacetylamino-phenol have shown. The filtrate was diluted to about 500 cc., heated, and then treated with hydrochloric acid until congo red turned color, causing the momentary separation of an oil which on stirring rapidly crystallized, forming bundles of pink microscopic platelets which when air-dried contained approximately two molecules of water of crystallization and melted at 103–5°. The yield was 17 g. When anhydrous the substance softens at about 125–30° and melts completely with decomposition at about 180°. It is readily soluble in alcohol, methyl alcohol, acetic acid and hot water, and in alkaline solution couples readily with diazotized sulfanilic acid.

Subs., air-dry, 0.6155: Loss, 0.0590 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{14}H_{15}O_5N_2As.2H_2O$: H_2O, 8.96. Found: 9.59.

Subs., anhydrous, 0.2355: (Kjeldahl), 12.55 cc. 0.1 *N* HCl. Subs., 0.3123: $Mg_2As_2O_7$, 0.1362.

Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48. Found: N, 7.46; As, 21.04.

***N*-(Phenyl-2-arsonic Acid)glycyl-4-aminophenol.**—Equimolecular quantities of *o*-arsanilic acid and *p*-chloroacetylamino-phenol yielded a dark colored solution from which an oil separated on cooling. This slowly solidified, especially after making definitely acid to congo red with hydrochloric acid. After standing in the ice-box the product was filtered off, washed, dissolved in dil. ammonia and the solution faintly acidified with acetic acid and treated with boneblack. On acidifying the hot filtrate to congo red with hydrochloric acid the arsonic acid again separated as an oil which soon crystallized. This substance was again dissolved in dil. ammonia and the solution acidified with acetic acid and again treated

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[1] THIS JOURNAL, 39, 1442 (1917).

with boneblack to remove the color which still persisted. On diluting the filtrate to about 300 cc., heating, and adding hydrochloric acid until congo red paper just turned and as long as the oily emulsion which momentarily formed redissolved, the arsonic acid separated on scratching as a heavy powder, consisting of short, colorless, microscopic platelets. The filtered substance was washed with water. The yield was 16 g. from 22 g. of *o*-arsanilic acid. When rapidly heated the acid darkens and then melts and decomposes at 208–9°. It is very sparingly soluble in boiling water and easily in boiling methyl alcohol or 50% alcohol.

Subs., 0.2331: (Kjeldahl), 12.9 cc. 0.1 *N* HCl. Subs., 0.2950: $Mg_2As_2O_7$, 0.1255.
Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48. Found: N, 7.75; As, 20.53.

(C) Derivatives of *m*-Arsanilic Acid.

***N*-(Phenyl-3-arsonic Acid)glycineanilide.**—(From *m*-arsanilic acid[1] and chloroacetanilide). On diluting the reaction mixture with water and rendering acid to congo red with hydrochloric acid the crystalline arsonic acid was gradually deposited. This was recrystallized first from 50% alcohol and finally from glacial acetic acid, separating from the latter as rosets of minute, cream-colored prisms which apparently contained solvent of crystallization. When rapidly heated to 215° and then slowly the dried substance darkens, then softens, and finally decomposes at 217–18°. It is rather sparingly soluble in hot water, but dissolves readily in hot 50% alcohol or acetic acid and is appreciably soluble in cold 95% alcohol.

Subs., 0.2422: (Kjeldahl), 14.25 cc. 0.1 *N* HCl. Subs., 0.2857: $Mg_2As_2O_7$, 0.1267.
Calc. for $C_{14}H_{15}O_4N_2As$: N, 8.00; As, 21.39. Found: N, 8.24; As, 21.40.

***N*-(Phenyl-3-arsonic Acid)glycyl-2-aminophenol.**—Although the reaction between *m*-arsanilic acid and *o*-chloroacetylamino-phenol was accompanied by the formation of *o*-amino-phenoxyacetic anhydride, as in the case of *p*- and *o*-arsanilic acids, the amount of anhydride was much less than that formed when the isomeric acids were used. Consequently the yield of the complex arsonic acid was much greater than in the case of the *o*- or *p*-arsanilic acid.

The reaction mixture from 22 g. of *m*-arsanilic acid and 19 g. of *o*-chloroacetylamino-phenol yielded an oil on cooling which redissolved on rendering the mixture ammoniacal, leaving about 3 g. of *o*-aminophenoxyacetic anhydride. The filtrate was acidified to congo red with hydrochloric acid, causing the deposition of a viscous oil which slowly crystallized on rubbing and letting stand. After standing for 24 hours in the refrigerator the crude substance was filtered off and washed with water. The deep colored solution of this product in dil. ammonia was neutralized with acetic acid and treated with boneblack. The still colored filtrate was diluted to about 300 cc., heated on the water bath, and then treated with hydrochloric acid until congo red turned color. On scratching and

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[1] This Journal, 40, 1583 (1918).

keeping sufficiently warm the substance slowly crystallized as almost colorless, flat, microscopic needles. If allowed to chill it separated first as an oil carrying coloring matter with it. If properly heated and with constant manipulation with a rod crystallization was almost complete in about 15 minutes.

After cooling it was filtered off and washed with water. The yield was 21 g. When rapidly heated to 185°, then slowly, the arsonic acid darkens and softens, finally melting and decomposing at 190–2°. It is sparingly soluble in cold water, more easily on boiling, and on cooling it again separates very slowly and incompletely. It is somewhat soluble in the cold in 50% or 95% alcohol, more easily on warming, and also dissolves in cold methyl alcohol or boiling acetic acid. A solution of the acid in strong ammonium acetate solution slowly deposits the ammonium salt as minute needles. Although hydrochloric acid precipitates the acid fairly completely from its salts as a gummy mass, an excess of acetic acid causes no immediate precipitate. However, on long standing the free arsonic acid separates slowly and incompletely from such solutions as a crust of broad, microscopic needles.

Subs., 0.1835: (Kjeldahl), 10.35 cc. 0.1 *N* HCl. Subs., 0.3004: $Mg_2As_2O_7$, 0.1282.

Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48. Found: N, 7.90; As, 20.57.

***N*-(Phenyl-3-arsonic Acid)glycyl-3-aminophenol.**—26.4 g. of *m*-arsanilic acid and 23 g. of *m*-chloroacetylamino-phenol yielded a purple oil which slowly crystallized on scratching. Attempts at purifying this substance by the usual method of reprecipitating the acid from its solution in dil. alkali by either acetic or hydrochloric acid were unsuccessful since the compound easily formed supersaturated solutions from which it separated extremely slowly, usually as highly colored, amorphous flocks. The substance was best purified by dissolving in hot 50% acetic acid and treating with boneblack, most of the purple color still persisting in the filtrate. On standing in the refrigerator the acid gradually separated as a thick crust of crystals which carried down the color with them. The yield was 27.5 g. A futher recrystallization was then attempted from 50% alcohol, the solution depositing the substance slowly as a light purple powder consisting of minute, irregular platelets and flat needles containing approximately 1.5 molecules of water of crystallization. When rapidly heated to 150° the anhydrous substance gradually sinters to a tar which decomposes at about 180–90°. In the cold it is more soluble in methyl alcohol than in the other solvents, but is fairly easily soluble in hot water, more so in hot alcohol, acetic acid or in these solvents when diluted. It is practically insoluble in acetone, benzene or ether.

Subs., air-dry, 0.3468: Loss, 0.0210 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{14}H_{15}O_5N_2As.1.5H_2O$: H_2O, 6.87. Found: 6.06.

Subs., anhydrous, 0.1607: (Kjeldahl), 8.95 cc. 0.1 *N* HCl. Subs., 0.2531: $Mg_2As_2O_7$, 0.1058.

Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48. Found: N, 7.80; As, 20.18.

***N*-(Phenyl-3-arsonic Acid)glycyl-4-aminophenol.**—The almost colorless oil obtained from 22 g. of *m*-arsanilic acid and 19 g. of *p*-chloroacetylamino-phenol could not be made to crystallize directly and was therefore dissolved by adding an equal volume of conc. hydrochloric acid to the reaction mixture, with chilling. On scratching, the clear solution deposited the hydrochloride of the arsonic acid as minute needles, the mixture setting to a thick mass after several hours. After filtering off, the hydrochloride was washed with 1 : 1 hydrochloric acid and was then suspended in water and dissolved by the addition of ammonia. The warm solution was treated with hydrochloric acid until acid to congo red, causing the partial separation of the substance as an oil which gradually crystallized on scratching. After standing in the refrigerator it was filtered off and washed with ice water. The yield was 21 g. When recrystallized from a small volume of hot water, in which it readily dissolves, it separates on rapid chilling as a milky emulsion which then very slowly crystallizes, partly as a hydrate. But if allowed to cool very slowly it separates gradually as microscopic platelets which are anhydrous. When rapidly heated the arsonic acid starts to sinter and darken above 170° and when held at 180° slowly shrinks together and decomposes. It is sparingly soluble in cold water but dissolves readily in the boiling solvent. It is easily soluble in hot alcohol, appreciably so in cold methyl alcohol, and but sparingly soluble in hot acetone. It dissolves in warm, dil. hydrochloric acid and on addition of the stronger acid it is converted into the hydrochloride, which separates slowly on rubbing.

Subs., 0.1527: (Kjeldahl), 8.47 cc. 0.1 *N* HCl. Subs., 0.3042: $Mg_2As_2O_7$, 0.1308.

Calc. for $C_{14}H_{15}O_5N_2As$: N, 7.66; As, 20.48. Found: N, 7.77; As, 20.75.

(D) Derivatives of Substituted *p*-Arsanilic Acids.

***N*-(2-Methylphenyl-4-arsonic Acid)glycyl-3-aminophenol.**—30 g. of the sodium salt of *o*-methylarsanilic acid (from *o*-toluidine) and 17 g. of *m*-chloroacetylamino-phenol, yielded an oil which rapidly crystallized on acidifying the mixture to congo red with hydrochloric acid. After dissolving the product in dil. ammonia and acidifying the solution with acetic acid, 17 g. of the pure arsonic acid separated as long, flat, microscopic needles. When heated to 285° the acid darkens and slowly decomposes. It is practically insoluble in boiling water, but is appreciably dissolved by hot 50% alcohol. An alkaline solution couples readily with diazotized sulfanilic acid.

Subs., 0.1338: 8.6 cc. N (28.5°, 763 mm.). Subs., 0.2924: $Mg_2As_2O_7$, 0.1182.

Calc. for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.72. Found: N, 7.31; As, 19.50.

***N*-(2-Methylphenyl-4-arsonic Acid)glycyl-4-aminophenol.**—This substance was obtained exactly as in the case of its isomer and in about the same yield. On acidifying a hot solution of the arsonic acid in dil. ammonia with acetic acid the free acid separates as microscopic, spindle-shaped needles. When rapidly heated it decomposes at 232–3° with preliminary darkening. It is very sparingly soluble in boiling water and slightly more soluble in hot 50% alcohol.

Subs., 0.1313: 8.6 cc. N (28.0°, 761 mm.). Subs., 0.3246: $Mg_2As_2O_7$, 0.1347.
Calc. for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.72. Found: N, 7.44; As, 20.01.

***N*-(3-Methylphenyl-4-arsonic Acid)glycyl-3-aminophenol.**—This substance was obtained as in the case of the two previously described compounds, starting with 2-methyl-4-amino-phenylarsonic acid.[1] Acetic acid slowly precipitates the compound from hot ammoniacal solution as aggregates of spindle-shaped micro-crystals. When rapidly heated it decomposes at 232–5° with preliminary softening and darkening. It is very sparingly soluble in boiling water or alcohol, more readily in hot 50% alcohol. An alkaline solution couples readily with diazotized sulfanilic acid.

Subs., 0.1682: 10.6 cc. N (21.0°, 755 mm.). Subs., 0.3100: $Mg_2As_2O_7$, 0.1275.
Calc. for $C_{15}H_{17}O_5N_2As$: N, 7.37; As, 19.72. Found: N, 7.28; As, 19.84.

***N*-(2-Carboxyphenyl-4-arsonic Acid)glycyl-3-aminophenol,** *o,p*-$HO_2C(H_2O_3As)C_6H_3NHCH_2CONHC_6H_4OH$(*m*-).—10 g. of 3-carboxy-4-amino-phenylarsonic acid,[2] were dissolved in 80 cc. of *N* sodium hydroxide solution (about 2 mols), then treated with 20 cc. of 2 *N* acetic acid and 8 g. of *m*-chloroacetylamino-phenol, and the mixture boiled for one hour. The reaction was apparently facilitated by the presence of the sodium acetate as buffer, since without the addition of acetic acid the solution would have reacted alkaline and decomposed the chloroacetylamino-phenol. On acidifying the clear, chilled solution with hydrochloric acid the reaction product crystallized. This was purified by redissolving in dil. sodium hydroxide, rendering faintly acid with acetic acid and adding boneblack in the cold to collect a small amount of flocculent material. The filtrate was warmed and then treated with an excess of acetic acid, the arsonic acid separating on scratching as thin, minute platelets. After washing with water and air-drying, the yield was 6 g. The acid separates with one molecule of water of crystallization and is practically insoluble in boiling water. It is somewhat soluble in hot alcohol or 50% alcohol and dissolves fairly readily in boiling methyl alcohol or glacial acetic acid. When rapidly heated the anhydrous substance darkens and swells, then decomposes at 204–7°. An alkaline solution couples readily with diazotized sulfanilic acid.

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[1] THIS JOURNAL, 40, 1588 (1918).

[2] Kahn and Benda, *Ber.*, **41**, 3862 (1908).

Subs., air-dry, 0.5776: Loss, 0.0236 *in vacuo* at 100° over H_2SO_4.

Calc. for $C_{15}H_{15}O_7N_2As.H_2O$: H_2O, 4.21. Found: 4.09.

Subs., anhydrous, 0.1441: (Kjeldahl), 7.1 cc. 0.1 *N* HCl. Subs., 0.3292: $Mg_2As_2O_7$, 0.1231.

Calc. for $C_{15}H_{15}O_7N_2As$: N, 6.83; As, 18.28. Found: N, 6.90; As, 18.03.

NEW YORK, N. Y.

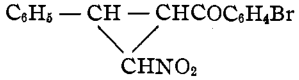
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

STUDIES IN THE CYCLOPROPANE SERIES. VIII. NITRO-CYCLOPROPANE DERIVATIVES.

BY E. P. KOHLER AND H. E. WILLIAMS.

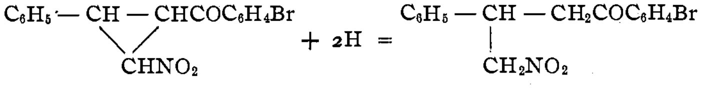
Received June 27, 1919.

In continuation of the work reported in the preceding paper of this series,[1] we have studied another nitro-cyclopropane derivative in the hope that a substance which would give more sparingly soluble products would enable us to isolate some of the intermediate compounds that baffled us in the earlier work. We selected for the purpose *p*-bromobenzoyl-phenyl-nitro-cyclopropane,

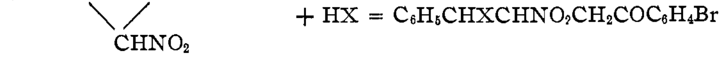


This nitro compound was made without much trouble by the method which had been developed for the bromine-free analog. It has 3 dissimilar asymmetric carbon atoms and 3 of the 4 possible stereoisomers were isolated in the course of the investigation. The structure of all of these is established by the fact that with various reagents they give products in which the carbon chain is not the same, showing that they are formed by opening a cyclopropane ring at different points.

On cautious reduction with zinc and alcohol all of the isomeric cyclopropane derivatives give the same substance that is obtained by addition of nitromethane to benzal-aceto-*p*-bromophenone. The ring is, therefore, opened between the carbon atoms holding the nitro- and *p*-bromobenzoyl groups:



The isomeric cyclopropane derivatives also combine very readily with the halogen acids but the ring is opened at a different point:



The reactions of the resulting halogen nitro compounds leave no doubt as to their structure. Thus the chlorine compound, when treated with

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[1] THIS JOURNAL, 41, 1379 (1919).